REDACTED DOCUMENTS RELATING TO DOCKET 7300

EXHIBIT G – Filed redacted

EXPERT REPORT

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ANNE CHRISTINE ROBERTS, M.D.

SANJEEVA KALVA M.D.

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I. INTRODUCTION

1. Plaintiffs' counsel on behalf of their clients who have been injured or damaged as the result of being implanted with certain Bard IVC filters have asked that we provide our expert opinions about the evidence surrounding the risks and benefits of those devices. We have been asked to render opinions to a reasonable degree of medical probability about the reasonable expectations of physicians who order the implantation of IVC filters and/or who implant IVC filters. This encompasses our reasonable expectations as Interventional Radiologists, who have also served as former consultants to Bard and other device manufacturers, experiences with the Medical Devices Section of FDA, service on various policy committees and leadership positions with the Society of Interventional Radiologists (SIR) and American College of Radiologists (ACR), professors and clinical instructors, chiefs of interventional radiology sections, consultants to physician colleagues, members on hospital formulary committees, and having all studied and authored peer-reviewed published literature on the subject of inferior vena cave filters (IVCF). We are asked to assess Bard's actions or inactions as relates to its marketing, testing, design, representations and concealment of important patient safety and effectiveness information it possessed about various iterations of Bard brands of permanent IVC filters with or without retrievable options.

2. We are interventional radiologists. We routinely treat patients with deep vein thromboses (DVTs) and pulmonary emboli, and we treat patients with indwelling IVC filters or patients who will be receiving these filters; we are intimately familiar with a variety of inferior vena cava filters including temporary, optional/retrievable and permanent filters.

3. We have been asked to provide our expert analyses and opinions on the following:

a. What information, including the severity, character and frequency of complications, would a practicing physician want and need to know concerning an IVC filter's safety and efficacy in order to conduct a proper (i.e., standard of care) risk/benefit evaluation for treatment of a patient? Considering patient safety is the primary concern and that open, honest and complete performance, safety and complaint data from manufacturers are required for physicians to fulfill their standard of care responsibility to provide informed consent to their patients;

b. Physicians' reasonable expectations of the requisite pre-clinical and clinical safety and effectiveness/risk-benefit evidence that is mandatory to justify widespread marketing of IVC filters for both temporary and permanent placements;

c. Data that Bard possessed, including testimony of witnesses regarding the Recovery, G2 and Eclipse IVCFs. What a reasonable physician's expectations, and acceptability of risks/complications versus benefits, were and are in view of such data and whether Bard met those expectations. These opinions, as with all others set forth herein, apply principles of medical standard of care which we believe should, apply to the standard of care and requisite principles to medical device manufacturers in the same or similar circumstances.

d. In our capacity as practicing physicians and members of SIR, what is the purpose and intent of the SIR quality control improvement and practice parameter publications, including the Society of Interventional Radiology

Standards of Practice Committee's *Quality improvement guidelines for the performance of inferior vena cava filter placement for the prevention of pulmonary embolism*, specifically the "thresholds" (Table 1) and "other trackable events" (Table 2) for these devices as found in medical articles published by the SIR/ACR, and whether Bard's characterization, use, and representations of these thresholds and trackable events was proper?

4. Medical devices, including IVC filters that are implanted in patients, have certain key functional parameters along with recognized complications. Key functional parameters that are often used to analyze IVC filters are recurrent pulmonary embolism (PE) rate, while maintaining caval patency. *See* Kinney, *Update on inferior vena cava filters.* J Vasc Interv Radiol 2003: 14:425-40. Filter complications may occur during insertion and during follow-up. It is the frequency, severity and type of complications that comprise the important data and information used by physicians and our professional society members to determine the devices or therapeutic options which are acceptable in making choices between and among available devices. The expectations of companies, like Bard, who market these devices to physicians who order and/or implant them, include complete honesty and accurate communication of any and all safety and effectiveness data and information they possess. Quoting Bard's former director of Regulatory Affairs:

> *"Transparency in matters that affect patient safety should be embraced as a primary corporate obligation."*
> (Christopher Ganser, Deposition Transcript, Oct. 11, 2016 (89:7-9), agreeing to statement from an article authored by one of its expert consultants, Dr. David Feigel).

5. Bard's one time Medical Director, David Ciavarella, M.D., and other employees of Bard, testified about the importance of providing all relevant data to doctors and allowing the

doctor to make risk/benefit determinations. Along with our own combined experience, education and training, our opinions are based on these articulated principles. (*See* Schedule 3-Testimony of Bard employees regarding the important of providing information to a physician to make a risk/benefit determination):

> *"The company needs to put the information out there in a way that it is relevant, understandable, not confusing to a physician about its product."*
>
> *"There is no higher duty that a device company has than to make sure the doctor has all the information he needs to decide whether or not he's going to put his patient at risk of this treatment, this device, or maybe he would choose something else…"*
>
> *"Expectations, acceptability of certain device and its risks and benefits, those are exclusively the rights of a doctor and a patient…"*
>
> *And if the doctor has a certain expectation about a device, it's important for him to have that information as to whether or not this device is going to meet his expectations…"*
>
> *"It has to be information that you know that doctors -- that are important to doctors and ultimately to patients in an informed consent decision about whether or not they should choose your product over some other alternative means of treating the patient*"
> (David Ciavarella, M.D., Deposition Transcript, Nov. 12, 2013 (91:23 -92:11, 92-95)

6. We need the safety and effectiveness data that companies possess from their testing and monitoring of their medical devices, especially implanted devices such as IVC filters, to allow physicians to provide full and fair balanced informed consent to patients for whom these devices are prescribed and indicated. The ultimate decision about acceptability of inherent IVC filter risk(s) rests with our patients as juxtaposed with the clinical benefit obtained by filtration, and they are entitled to full disclosure of all material information that companies possess about the safety, performance, design and complications of recommended medical devices when it comes to rendering these decisions.

7. The reasonable expectations physicians and patients have of medical device companies, like CR Bard and Bard Peripheral Vascular, who market these devices to physicians

who order and/or who implant them, include complete, honest and accurate, and frequently updated communications of any and all safety and effectiveness data and information the companies possess and to allow physicians to properly and completely fulfill their obligations of informed consent. This information is required by physicians in making appropriate therapeutic decisions on behalf of their patients where an IVC filter may be indicated or considered as a therapeutic option. This includes the expectations of what a reasonable patient and physician would want and need to know in the same or similar circumstances for which an IVC Filter has been prescribed, considered or recommended.

8. The ACR–SIR PRACTICE GUIDELINE ON INFORMED CONSENT FOR IMAGE-GUIDED PROCEDURES (Rev. 2016). These same principles, although possibly stated differently in prior publications of this Practice Guideline, have remained constant throughout the relevant time periods we address in this report. This Practice Guideline calls for informed consent for all invasive procedures, and states in pertinent part:

> Prudent and ethical medical practice requires close communication between the patient and the physician. If the patient is unable to provide consent, the patient's legal representative or, in the case of a minor, the patient's parent(s) or legal guardian, represents the patient in the consent process. The patient or representative and, when appropriate, the patient's family must have every opportunity to understand the treatment or procedure the patient is to receive and its reasonable risks, benefits, and alternatives; to have all questions answered; and to fully consent to the treatment and procedure.
>
> I. Introduction
> This guideline was revised collaboratively by the American College of Radiology (ACR) and the Society of Interventional Radiology (SIR). Prudent and ethical medical practice requires close communication between the patient and the physician. The patient, or if the patient is unable to provide consent, the patient's legal representative and, when appropriate, the family, must have every opportunity to understand the treatment or procedure the patient is to receive and its reasonable alternatives, to have all questions answered, and to fully consent to the treatment and procedure. The degree of disclosure required for a valid consent varies from state to state, but there are two generally

recognized standards. The first is measured by what a reasonable physician in his or her professional judgment believes is appropriate to disclose to the patients. The degree of disclosure depends on perceptions of the physician in each case. The second standard is based on what a reasonable patient would want to know in the same or similar circumstances.

The trend is toward the "reasonable patient" standard, which usually requires greater and more detailed disclosure of information.

…

B. Protocol for Informed Consent for Elective Procedures

1. Before the proposed procedure is performed, the following will be explained to the patient or, if the patient is unable to provide consent, to the patient's legal representative:

a. The purpose and nature of the procedure or treatment.

b. The method by which the procedure or treatment will be performed.

c. The risks, complications, and expected benefits or effects of such procedure or treatment.

d. The risk of not accepting the procedure or treatment.

e. Any reasonable alternatives to the procedure or treatment and their most likely risks and benefits.

f. The right to refuse the procedure or treatment.

See https://www.acr.org/~/media/1A03224CA4894854800C516012B6DB5A.pdf.

9. As physicians caring for patients who are candidates for IVC filters, or have them implanted, we must provide our patients with full informed consent, specifically the risks, complications, and expected benefits or effects of such procedure or treatment. In order to fulfill this obligation to our patients, the companies who manufacture, market and sell IVC filters, including Bard, must provide current and *up-to-date* safety information regarding the frequency, severity and type(s) of complications associated with their specific filter(s). The more severe the injury or complication, the greater the urgency, and oftentimes, immediacy to act and advise. With this vital information, physicians can decide whether his or her patient is appropriate for IVC filter placement and, if so, which specific filter should be implanted.

10. The experience of other physicians with the use of medical devices, especially relatively new devices, and particularly when no controlled clinical trials exist that establish data for long term safety and effectiveness, is extremely important information which must be shared with other physicians. Often such experiences are shared by way of case reports written in medical journals, presentations at local or national interventional meetings reviewing complications, and by way of reports of adverse events and device-related injury reports to product manufacturers like Bard.

11. Time is of the essence when dealing with a company's design concerns that relate to unexpected and unintended consequences of medical devices like IVC filters which are implanted in the largest vessel in the human body - a direct pathway to the heart and in close proximity to the aorta, duodenum and pancreas, kidney, vertebra, and liver, and which can put our patients at risk for potentially fatal consequences should the device fail to remain stable and intact. There is nothing more important to physicians who order or implant IVC filters than to be kept continually apprised of design and performance problems or safety concerns by other physicians and the company that is selling the product.

12. Our expert opinions are based on medical standard of care principles and how those principles relate to the expectations of what a reasonable patient and physician would want and need to know in the same or similar circumstances for which an IVC Filter has been prescribed, considered or recommended.

13. These opinions are derived from our experiences as authors of guidelines and consensus statements, members of Society of Interventional Radiologist (SIR), clinical and pre-clinical experience, training, education, teaching, writing, presentations, and peer reviewed literature, interactions with physician colleagues, patients and IVC filter manufacturers.

14. We apply the same analyses and methodology in reaching these kind of opinions as we apply in our professional, clinical and teaching capacities and in many respects in our research, writing and submitting medical articles to peer-reviewed journals and publications.

15. We have reviewed and considered the expert reports of David Kessler, M.D., Robert McMeeking, Ph.D., Robert Ritchie, Ph.D., Mark Eisenberg, M.D., and Rebecca Betensky, Ph.D. We intend to also review and consider the expert reports submitted by experts retained by Bard in this matter, which we understand will be forthcoming in approximately 30 days. We reserve the right to supplement this report once we have the opportunity to review that additional information.

II. SUMMARY OF QUALIFICATIONS

A. <u>Thomas Kinney, M.D., M.S.M.E</u>

16. I am a Clinical Professor of Radiology at the University of California, San Diego (UCSD).

17. I have a BS degree in physics with a minor in mathematics from Clarkson University (1978).

18. I was hired by Bell Laboratories and offered graduate education, obtaining a Master of Science in Mechanical Engineering in 1979 at Stanford University.

19. I worked for NASA-Ames Research center for 2 years, 1979 - 1981, and worked as a design engineer for Dr. Thomas Fogarty, 1979 - 1983. In this latter position, I designed, tested and submitted for FDA 510K approval several catheters and surgical clamps.

20. While in medical school at UCSD from 1983 - 1987, I also designed, tested, and manufactured surgical instruments for Dr. Pat Daily, including one device for which 510(k)

clearance was received from the FDA [External cooling pad for assisted cardioplegia/hypothermia].

21. I did my medicine internship at UCSD from 1987 to 1988 and served my radiology residency at Massachusetts General Hospital (MGH) from 1988 - 1992. In this residency, I did a sub-fellowship for one year in body imaging and intervention. I also completed a vascular and interventional radiology (IR) fellowship at MGH from 1992 - 1993.

22. I worked one year in private practice radiology doing IR and diagnostic radiology in Long Island, New York and then came to UCSD in 1994. I have practiced interventional radiology at the University of California at San Diego for the past 23 years. In 2008, I became the director of the UCSD Hereditary Hemorrhagic Telangiectasia (HHT) clinic (a center of excellence for treatment of patients with HHT).

23. I have been interested in inferior vena cava filters (IVCF) for many years starting with my fellowship at MGH and published a review article (2003) and many standards relating to IVCFs (See Schedule 5). I have served on the SIR technology assessment committee which has been interested in the performance characteristics of filters, in particular, retrievable filters. I have consulted with Bard in instructing other physicians on how to insert the Recovery filter (RNF) and retrieve it, and I also participated in animal experiments along with Dr. John Kaufman with the G2 and G2X/Express filters.

24. I was also a paid consultant for Bard for telephone consultations with regard to difficulties with the Bard filters. I participated in a meeting in Chicago, Illinois when a group of interventional radiology physicians were collected to discuss issues with filter complications, specifically fractures and migrations. I served as chairman of the Data Safety Monitoring Board for the Crux Filter [a retrievable IVC filter] and was on the Data Safety Monitoring Board on the

Angel Filter [A tethered temporary filter inserted from a femoral site that can also be used for venous access]. In the role of Data Safety Monitor Chair for the Crux trial, I was responsible for halting the trial after filter fractures were identified and design changes were implemented and the trial successfully restarted.

25. My opinions are based on my knowledge and expertise of IVC filters and my own personal experience with Recovery and G2 filters and documentation, data, and evidence I have seen for the first time in 2017. Plaintiffs' counsel has provided me open access to a database that contains Bard internal documents and depositions of Bard employees, past and present. I have also been provided with the expert report of Dr. David Kessler, former commissioner of FDA; the expert biostatistics report of Dr. Rebecca Betensky; Engineering reports of Dr. Robert McMeeking and Dr. Robert Ritchie.

26. Had I been aware of this evidence I would not have used the early Bard devices (RNF and G2), nor would I have agreed to act as a paid consultant to Bard. I would have recommended a long-term follow-up study of the RNF as recommended by Dr. Asch to better understand and document performance characteristics of this filter. I would have strongly urged Bard to not launch RNF and G2, or to immediately recall both products very shortly (3-4 months) after releasing each for widespread use based on the adverse complications and injuries that were being reported by many of my colleagues and Bard's internal analyses of same.

27. My billing rate is $700 per hour.

28. I have reviewed the material referred here in and listed in our Facts and Data Considered, Appendix A.

29. I understand I may be called upon to offer opinions in rebuttal to experts designated by Defendants.

30. A true and accurate copy of my current CV, including a list of our publications for the last 10 years, is attached as Appendix B.

31. My testimony in legal matters for the past four years is listed in Appendix C.

B. <u>Anne Roberts, M.D.</u>

32. I am the Division Chief Vascular and Interventional Radiology and Clinical Professor of Radiology at the University of California San Diego School of Medicine School (UCSD).

33. I have a BA degree in History from University of California, Los Angeles (1972). I also have a MA degree in History from the University of California, Los Angeles (1973)

34. I have a medical degree from University of California San Diego, School of Medicine (1982).

35. I did my medicine internship in Obstetrics and Gynecology at Cedar-Sinai Medical Center in Los Angeles in 1982 - 1983, and served my diagnostic radiology residency at Massachusetts General Hospital from 1982 thru 1986. I did my vascular and interventional radiology fellowship from 1986 – 1987 at Massachusetts General Hospital.

36. I spent a sabbatical year working at the Food and Drug Administration (FDA) in the Division of Cardiovascular, Respiratory, and Neurological Devices (Office of Device Evaluation) in the Center for Devices & Radiologic Health (CDRH). During that year I was involved in evaluating many devices prior to them coming to market. After completing my sabbatical, I served on the FDA's Circulatory System Devices Panel.

37. I have been active in the Society of Interventional Radiology serving on multiple committees and offices including serving as the President of the Society in 1996-1997.

38. I also served as a Trustee on the American Board of Radiology. I was elected to the Council Steering Committee of the American College of Radiology and have also served for 6 years on the Board of Chancellors.

39. My particular interests center on interventions in women. I have been very active in treatment for fibroids including uterine artery embolization, and MR guided focused ultrasound. I am involved in treating women with pelvic congestion syndrome, and invasive placenta of the uterus. Opening up fallopian tubes in patients with infertility and also performing percutaneous fallopian tube obstruction (ESSURE device) for those women done with childbearing are also procedures in my areas of expertise.

40. I have also had a long interest in IVC filters. My first research project as a resident/fellow was working on the clinical follow-up of the Bird's Nest Filter as part of the clinical trial for FDA approval. I have maintained my interest in IVC filters giving many talks on various aspects of IVC filters, as well as multiple publications, the most recent being a review article on vena cava filters for UpToDate, the latest peer reviewed version to be published in 2017 (*See* Schedule 5).

41. I served as chair of the Data and Safety Monitoring for the Denali filter which is manufactured by Bard.

42. My billing rate is $750 per hour.

43. I have reviewed the material referred here in and listed in our Facts and Data Considered, Appendix A.

44. I understand I may be called upon to offer opinions in rebuttal to experts designated by Defendants.

45. A true and accurate copy of my current CV, including a list of our publications for the last 10 years, is attached as Appendix B.

46. My prior testimony in legal matters for the past four years is listed in Appendix C.

C. <u>Sanjeeva Kalva, M.D.</u>

47. I am an Associate Professor of Radiology and Chief of Interventional Radiology at the UT Southwestern Medical Center.

48. I have a medical degree from Kurnool Medical College, Vijayawada University of Health Sciences in Kurnool, India (1993).

49. I did my medicine internship at Government General Hospital in Kurnool, India, 1993 and did my diagnostic radiology residency at Nizam's Institute of Medical Sciences in Hyderabad, India from 1996 thru 1998. I completed my vascular and interventional radiology fellowship at Koval Medical Center and Hospital, Coimbatore, India in 2000.

50. I worked for Harvard Medical School as a researcher in 2004, studying abdominal imaging and interventions at Massachusetts General Hospital. I completed a vascular and interventional radiology fellowship at Massachusetts General Hospital in 2006, and after completion I was recruited to join the Harvard faculty. I spent a decade at Harvard caring for patients, teaching, and conducting cutting-edge research in IR before joining the UT Southwestern faculty as Chief of Interventional Radiology in 2013.

51. I have led multiple research studies and publishing book chapters, two books, and many peer-reviewed papers. I have helped establish standards of care for my peers in the field, including the use of inferior vena cava filters and the management of aortic disease. I am actively involved in education, teaching IR to medical students, residents, and fellows and offering interdisciplinary lectures to physicians whose specialties overlap with IR.

52. I have won numerous awards for my clinical, teaching, and research acumen. I was privileged to receive the Dr. Athanasoulis Award for Excellence in Teaching and the Outstanding Performance Award for excellence in patient care and teaching while at Massachusetts General Hospital. In 2012, I was honored to be named as Fellow of the Society of Interventional Radiology.

53. My billing rate is $700 per hour.

54. I have reviewed the material referred here in and listed in our Facts and Data Considered, Appendix A.

55. I understand I may be called upon to offer opinions in rebuttal to experts designated by Defendants.

56. A true and accurate copy of my current CV, including a list of our publications for the last 10 years, is attached as Appendix B.

57. I have never testified in any legal matter.

III. OPINIONS

58. As physicians with patients who are candidates for IVC filters, or have them implanted, it is our opinion that in the interest of patient safety, informed consent, risk-benefit considerations and analyses, medical and scientific ethics and honesty, that reasonable members of SIR, ACR and other medical doctors who prescribe or implant IVC filters would expect the following clarity, detail, alerts, warnings and action by Bard:

59. The failure of the Recovery Filter device to maintain adequate migration resistance when the hooks are not engaged raises questions about potential safety and effectiveness of the device. Bard should have not sold this device until it adequately studied and

resolved that issue, or should have advised physicians of this potential fixation problem and ensuing failure existed. They did not.

60. [redacted]

61. [redacted]

62. [redacted]

[redacted]

63. We fully endorse Dr. David Kessler's opinion that:

a. "A prudent device manufacturer having questions about the safety of their device would wait for test results to come back before engaging in a "Full Market Release." Moreover, if the test showed poorer migration resistance performance than existing devices on the market, a prudent manufacturer would hold off on a full market release pending resolution of the problem."

b. A clinical study of the long-term performance of the Recovery Filter (as compared to the retrievability study performed by Dr. Murray Asch) would have identified issues related to migration, filter embolization, filter fractures, filter tilting, and perforations; Dr. Asch's testimony indicates that Bard had originally planned such a study.

c. Bard should not have marketed the Recovery Filter after December 5, 2003. Bard should have postponed until resolution of the device's safety issues raised by its migration resistance tests.

d. [redacted]

e. Bard should have continued the distribution hold on the Recovery Filter after it learned of statistically significant evidence that the filter posed an increased risk compared to certain other filters, including the SNF, and

that the filter was less migration-resistant in preclinical tests than the SNF predicate.

f. [redacted]

g. [redacted]

h. [redacted]

64. Reasonable interventional radiologists and other physicians agree that "when assessing the significance of a safety risk, it is important to look at the totality of the scientific

evidence." It was not only the increased reporting rates of adverse events associated with the Recovery Filter or the poorer migration resistance testing results of the filter, but most importantly, the totality of evidence, including both the increased reporting rates (or the rapidity of reports) of adverse events and the poorer migration resistance results especially given the relatively short filter dwell-times over which these reports were occurring.

65. We also endorse Dr. David Kessler's opinions that:

a. [redacted]

b. [redacted]

and migration or embolization resistance should have been recognized as crucial design tradeoffs for the RNF.

c. Bard had an obligation to share information derived from their safety analyses utilizing adverse event reporting rates in conjunction with preclinical testing with patients and physicians, including members of SIR, ACR and all societies of professionals responsible for inserting filters or ordering filters- pulmonary, hematology/oncology, family medicine, cardiology, and vascular surgery. This information must be shared in order for physicians to make proper decisions concerning the risks and benefits of using an IVC filter device in particular patients depending upon their clinical circumstances.

d. Reasonable interventional radiologists, members of SIR and ACR, and other physicians who prescribe and/or implant IVC filters expected Bard would have shared and been completely open when it "determined that there was evidence of an increased adverse events reporting rate of embolization deaths, migrations, and filter fractures associated with the Recovery Filter compared to the SNF filter," and that "this increase in reporting rate, according to Bard, was found in conjunction with poorer migration resistance testing results of the Recovery Filter compared to the SNF Filter."

66. In regards to the G2 Filter, reasonable interventional radiologists, cardiologists, members of SIR and ACR, and physicians who prescribe and/or implant IVC filters should have been advised by Bard the following findings described by Dr. David Kessler:

a. Bard began working on a development project to reduce fracture complication from the Modified Recovery (G2) device. Bard's Modified Recovery (G2) filter is electropolished and passivated, and evidenced to be more corrosion resistant than the G2 passivated filter.

b. Dr. Betensky's findings of a statistically significant increase in the risk ratio for migration, perforation, and tilted filter with the Modified Recovery (G2) compared to SNF filters is important in light of Bard's preclinical caudal push test results that showed that the Modified Recovery (G2) performed worse than the SNF and RNF filters.

67. We also endorse Dr. Kessler's opinion that "[t]his iterative process put patients at risk because Bard failed to assure that the filters it placed on the market did not raise new safety questions. Bard was "beta testing" its IVC filters in patients." In effect, Bard was using compromised filter designs to obtain serial FDA clearance for iterative filter design improvements.

68. Based on the materials and information considered by Dr. David Kessler, it is also our opinion, that

a. Bard misrepresented in its sales and marketing materials, "Dear Doctor" letters, and internal statements/directives to its sales force that:

i. a) its Recovery and Modified Recovery (G2) filters were equivalent to or more migration resistant than the SNF, "older filters" and competitor filters such as the Greenfield, VenaTech, OptEase and TrapEase;

ii. b) movement or migration of the filter was a known complication of vena cava filters;

iii. c) its Recovery and Modified Recovery (G2) filters were marked improvement over currently available devices and were the latest advancement in filter technology; and

iv. d) that its Modified Recovery (G2) filter took strength and stability to a new level.

b. It was misleading for Bard's Modified Recovery (G2) Filter IFU's to omit mention of the statistically significant increased reporting rate of deaths related to weaker migration resistance observed in the Recovery Filter.

c. In the face of known safety risks, and internal analyses of evidence of increased risk as documented above, Bard had an obligation to reduce the risk of harm to those patients who had/have the device implanted.

d. As soon as Bard was aware of safety risks, and internal analyses of increased risks as documented above, Bard had an obligation to develop a strategy to effectively detect problems with the Recovery and Modified Recovery (G2) filters and reduce the risk associated with those problems in patients who had the device implanted, and during that period of time Bard should have not have sold these devices to interventional radiologist, members of SIR and ACR, or any physician who prescribes or implants IVC filters.

69. We are concerned about retrievable IVC filters remaining in patient after the patient is no longer at risk for pulmonary embolism; especially when a filter that was designed as retrievable and is used as a permanent device. Patients were put at increased risk when Bard designed the Recovery and Modified Recovery (G2) filters to be retrievable, but marketed them for permanent use. Other than in-vitro testing of their filters, limited animal models (all with relatively short indwell times) and modeling techniques such as Finite Element Analyses and Fatigue tests with assumed and under-loaded conditions, there was no solid base of data to understand the long-term performance of such a filter, or the length of the retrievability window. In effect, physicians were inserting these filters with presumptive belief that Bard had solid pre-clinical and clinical evidence of the long-term performance characteristics of these filters.

70. We also agree that if Bard wanted to sell a device as a retrievable filter with different technology, allowing for retrievability, but labeled for permanent use, it should have conducted clinical studies to evaluate the safety and efficacy of this device as permanent device. If Bard wanted to sell a permanent device with a retrievable option having different technology compared to prior filters, it should have conducted clinical studies to evaluate the long-term safety and efficacy of this new device, including the risks associated with prolonged insertion and how long the filter could be left in without risk to a patient's safety.

71. Bard had an obligation to take steps to protect existing patients from the risks associated with Recovery and G2 filters.

72. Bard failed to provide patients and doctors with information about appropriate monitoring and evaluations (including radiologic studies) that could identify and protect against adverse events. Such information was especially important in light of the risks, discussed in this report, associated with the Recovery and Modified Recovery (G2) filters.

73. Physicians were not told that Bard failed to conduct sufficient research and testing to understand how the IVC filter functioned, and failed to conduct pre-market testing that would determine how the device would function when used in a reasonably foreseeable manner. If Bard had disclosed the information discussed within this report, reasonable physicians would not have used these devices.

74. [redacted]

75. It is our opinion that Bard lacked important safety information when it began marketing each of their IVC filters regarding the risk of complications associated with their IVC filters and, once on the market, failed to provide practicing physicians with timely and updated information of these risks including, without limitation, adequate information related to the character, severity and frequency of the Recovery, G2/G2X and Eclipse IVC filter's high complication rate in relation to its competitors and its own products, including the SNF filter. This lack of information precluded physicians from evaluating the risk-benefit analysis for their patients. If Bard had disclosed the information discussed within this report, reasonable physicians would not have used these devices.

76. Based on our education, training, experience and practice, it is our opinion, to a reasonable degree of medical probability that physicians would want and need to know any potential adverse complications for a device on the market, especially if the complications are

life threatening, in order to properly perform a risk-benefit analysis of the device for treatment in patients.

77. In addition to our opinions set forth above, we are prepared to testify as to our own observations and impressions as interventional radiologists with patients who are candidates for IVC filters, and have them implanted.

IV. EARLY WARNING SIGNS ABOUT THE RECOVERY NITINOL FILTER (RNF)

A. Kaufman, et al. Study

78. The first report of the RNF occurs in 2000 in abstract form (JVIR 2000 (supplement) 11: 195-196). In this abstract, Dr. Kaufman, Venbrux and Brown describe animal studies (18 adult female Dorset or Suffolk Sheep (mean weight 99 +/11 pounds). They describe the filter made of nitinol made of six (6) centering arms and six (6) legs with elastic anchoring hooks. *In vitro* the filter withstands a 70 mm Hg pressure gradient in a **21 mm** diameter tube without migration and traps emboli equivalent to current permanent filters. Retrieval is from jugular approach using a new grasping cone device. Twenty four filters were inserted in the 18 sheep. Cavograms and pathology of IVC and adjacent structures were obtained in all animals. Four groups were studied:

a. Three (3) animals sacrificed after deployment and immediate retrieval;
b. Three (3) animals sacrificed at 4 weeks after deployment with immediate retrieval;
c. Six (6) animals sacrifice after removal at twelve (12) weeks implant time;
d. Six (6) animals, sacrifice eight (8) weeks after removal at twelve (12) weeks implant time.

79. Findings from Kaufman, *et al*. (2000):

a. All deployments were successful.

b. Two filters were deployed in each animal in groups A and B 24/24 filter retrievals were successful including 12 removed after 12 weeks implant time (groups C &D). The IVC was patent in 24/24 animals at follow-up cavography, with no major device migrations.

c. The IVCs in groups A & B had minimal gross and microscopic abnormalities at points of filter contact, limited in depth to the subadventitia.

d. Gross exam of IVCs in groups C & D revealed limited fibrosis at points of contact between the filter and IVC, with partial resolution in group D.

e. Probable transmural incorporation of hooks was noted in some cases. Microscopic exam of the 12 weeks IVCs is pending.

f. CONCLUSION: In a sheep model this IVC filter can be successfully removed acutely and up to 12 weeks following implantation with limited residual abnormality of the IVC.

Kaufman, et al. *Scientific Session 9 Venous Thromboembolic Disease*, February 2000Volume 11, Issue 2, Supplement, p1-535

Important points from this study were it was inserted in relatively small cavae (average 21 mm diameter) and used as the upper threshold of pressure resistance to migration of 70 mm Hg. These factors become important later when the filter is used in a cava up to 28 mm in diameter and the pressure threshold is reduced to 50 mm Hg.

80. An early instance of migration was investigated by NMT Medical in a report dated September 1, 2000 (later acquired by Bard Peripheral Vascular and conducted by employees of both entities before and after acquisition). (09/01/2000 R&D Technical Report, BPVE-01-00054540). This occurred in the study initiated by Dr. Asch (see below). No mechanical failure property was found, the filter was intact without fracture and the migration was attributed to a massive embolic load or force on the filter. At the time, there had been eleven (11) RNF inserted and one (1) migration that is a 9% migration rate with the Recovery Filter.

81. This is a concerning statistic. It should have immediately put Bard on notice that they needed to further characterize the true rate of such occurrences. And, if such rates of bulk migration were documented, Bard should have reconsidered and reevaluated the design of Recovery Filter, which at the time was a concept device and physically different than the Recovery Filter's predicate device, Simon Nitinol Filter (SNF).

B. The Dr. Asch Study

82. The study performed by Dr. Murray Asch (Radiology, 2002; 225:835-844) reports on the initial experience in humans with a new retrievable inferior vena cava filter (IVCF). The device was released in Canada on a special-access basis by the Health Protection Branch of the federal government of Canada (Ottawa, Ontario) and use approved by the University of Toronto ethics department and institutional review board (IRB). *Asch Study, Initial Experience in Humans with a New Retrievable Inferior Vena Cava Filter*, 2000

83. This was a small study designed to evaluate the retrievability of the RNF. Thirty-four (34) consecutive patients who required an IVC filter and who were anticipated to return to anticoagulation therapy (10 days to 12 weeks post procedure) or to not need therapy between 10 days and 12 weeks were selected to receive a Recovery Filter between April 2000 and November 2001. The Asch study was prospective multi-institutional with all the filters being inserted by the Principle Investigator (Dr. Asch). Two patients were excluded from the study because of anatomic conditions unfavorable for filter placement-one patient had a 33 mm diameter cava (too large for the RNF) and another had congenital interruption of the IVC (with hemiazygous continuation) so the total number of patients was 32. Abdominal radiographs were obtained 1 and 7 days after placement per protocol and the filters retrieved via jugular access when it was felt the patient could safely resume full and uninterrupted anticoagulation. In any patient in

whom an adverse event was clinically evident, appropriate imaging was undertaken. At the 10^{th} patient, routine follow-up abdominal radiographs were obtained for "possible" migration. This change in protocol occurred because of unsuspected migration of the Recovery Filter in patient 9. The mean age of their patients was 53 years (range, 18-83 years).

84. There were 16 male and 16 female patients. Deep vein thrombosis (DVT) was found by ultrasound in 23 patients (18 RLE DVT, 5 LLE DVT) and pulmonary embolism (PE) was present in 15 patients detected by CT Scans of the Chest with contrast (CTA). There were two patients who had filters placed for prophylaxis (i.e., no DVT or PE at insertion, but with medical conditions placing them at high risk for DVT and possible PE). There were some technical difficulties during insertion in a majority of cases (one could not be advanced through the introducer sheath and in 17/23 filters there was some difficulty releasing the filter legs from the splines of the stabilizer arm). This was resolved by gentle twisting motion of the introducer sheath and was attributed to a manufacturer polishing procedure which rolled over the edges of the splines. Twenty (20) filters were placed via the left femoral and 12 via the right.

85. The results of the Dr. Asch study, i.e., this early Recovery Filter study, demonstrated filter tilting (>15°) occurring in two patients (6%) of 32 deployments. In each of the two cases the tilt was 20° and toward the side contralateral to the puncture. No patient developed symptomatic PE or insertion-site DVT after filter placement or from retrieval.

86. Seven (7) patients were found to have trapped thrombus in the filter (22%).

87. In three (3) patients the thrombus in the filter was felt to be small and they were removed without difficulty. Two filters had large thrombus at the time of removal.

88. In one patient the filter had migrated approximately 4 cm cephalad (towards the head or heart) at the time of elective removal, 17 days after insertion (migration on an earlier

radiograph (4 days earlier) had been missed initially but was seen retrospectively). A larger size sheath (20 Fr compared to the usual 10 Fr) was used to remove this filter and thrombus.

89. All attempted retrievals (24) were successful, with retrievals spanning from 5-134 days (mean, 53 days). They performed follow-up in 22 (92%) of the 24 patients who underwent retrieval and one patient developed clinical symptoms of PE 133 days after filter removal but CTA did not depict PE.

90. In the discussion of this article, Dr. Asch indicates "the perfect temporary IVC filter would have high clot-trapping efficacy and low incidence of caval thrombosis. It would have to be non-migratory yet be able to be retrieved at a time distant from insertion. Finally, there should be no tether to limit patient mobility or serve as a nidus for infection. While intimal hyperplasia is expected to occur with any implanted device, there are filter design factors that would limit the associated adverse effects." [It should be pointed out that at the time a trial evaluating a tethered filter (Tempo Filter by B. Braun) was also being performed. This filter was inserted via the right jugular vein and tethered through the venous system by a wire and was removed after a period of several days. The trial of the Tempo Filter was stopped because of issues with migration to the right atrium]. It was the author's hypothesis that the ability to retrieve the RNF without concern for hyperplasia required the filter to have little metal contact with the caval wall. He recognized that the design of the Trapease filter and Gunther tulip would possibly allow intimal hyperplasia making retrieval more difficult or even impossible. "The design of the RNF allows for the filter arms to slide out of any potential sleeve once elastic leg hooks have been removed from the caval wall." This is often described by the following analogy: "as if a foot was being removed from a sock". He also considered that since intimal

hyperplasia stabilized at approximately 3-6 weeks, one would expect that beyond that time, filter fixation would not be an issue.

91. In the single migration Dr. Asch reported, there was a large trapped embolus in the filter and presumably this was felt to be the cause of the migration. This was evidence that the design of the Recovery Filter used in that study had the potential of becoming unstable when encountering the type of embolic insult or embolic load. Or, it might be related to erroneous assumptions of caval the dynamics (caval pressures and diameters, specifically). This clot trapping ability is a key attribute by which IVC filters are evaluated. The ideal filter should trap the life-threatening embolus and maintain stability in position within the IVC. Our review of documentation produced by Bard showed no evidence of a similar design failure in Bard's predicate device, SNF, after having been on the market since 1995 and implanted in thousands of patients[1]. They noted one additional patient with filter arms outside of the vena cava (at venography and CT). This patient was asymptomatic and had the filter removed at 134 days. He had undergone an abdominal surgical procedure and filter penetration of the cava was considered to be due to this surgical manipulation in the region of filter implantation.

92. This instance of migration was investigated and described in a report dated September 1, 2000. No mechanical failure property was found, the filter was intact without fracture and the migration was attributed to a massive embolic load or force on the filter. At the time, there had been eleven (11) Recovery Filters inserted with one (1) migration; or a 9% migration rate with the Recovery Filter. This migration of 4 cm towards the heart was detected by the study requirement of follow-up radiographs. Note, if this radiograph had not been obtained or the retrieval attempted when it was, this filter could have potentially migrated

[1] SNF had been available since 1990, and had undergone various design changes, including in 1995. SNF was used as a predicate device for the Recovery Filter.

centrally with potential serious life-threatening complications. Comparison of migration rates with other filters were made by Dr. John Kaufman.

93. Dr. John Kaufman, an IVC filter expert, and a key opinion leader for Bard, was among the reviewers and "had major concerns that filters do not migrate very often (1% or less in his experience) and that this was the first time a filter was challenged and it migrated, albeit only to the suprarenal level. His concern was that "we are a victim of low numbers, that this was the first and only incident and that it is impossible to predict what would happen to the next filter when challenged?"

94. It was decided the study at Mt Sinai Hospital, where Dr. Asch practices, would resume (after full disclosure to patients involved in the study and further informed consent that included information about this 4cm migration of another test subject), and if another "major" migration (>2 cm) occurred, the study would stop and re-evaluation of the filter design undertaken.

95. As practicing physicians, we reasonably assume Bard would not risk implanting the Recovery Filter if further evidence suggested Patient No. 9's experience was not an aberration, or further evidence suggested the current design of RNF did not eliminate this potentially fatal risk.

96. This same protocol, "another migration" and we'll stop the study, and concern for patient safety should have been adapted as a safety standard followed by Bard once they made the decision to sell this device without further testing and design changes in the open market.

97. Dr. Asch's 2002 radiology study can be summarized as follows:

a. There were two (2) tilted filters, one (1) migration with trapped thrombus and one (1) asymptomatic caval perforations or four (4) complications or 12.5 %.

b. The filter trapped thrombus in 7 cases showing effectiveness and was retrieved in all attempts. None of these trapped thrombi were of the size and quality of the clot that disrupted the fixation and stability of the filter as was seen in Patient #9, which is the type of clot for which RNF was expected to stop and retain in the location. Regardless of the size of embolic insult, the retrievable filter should maintain stable caval positioning.

c. The study proved retrievability without any caval damage from the procedure.

d. Dr. Asch's study was designed to study retrievability; the study was neither designed nor sufficiently powered to study the long-term performance of the Recovery Filter. Notwithstanding, potential serious concerns should have arisen about possible performance characteristics of the long-term (permanent) implantation of the Recovery Filter.

e. This should have prompted Bard to revisit the design features of Recovery Filter, and initiate a safety and effectiveness clinical trial to gain knowledge about the long-term safety and effectiveness of Recovery Filter, especially if Bard's plan was to market the Recovery Filter as an optional retrievable and permanent device.

f. According to Dr. Asch's deposition, Bard promised it would do both before releasing the Recovery Filter into the marketplace, i.e., make appropriate design changes and conduct a long-term safety and effectiveness clinical trial. *See* Murray Asch, M.D. Deposition Transcript, May 2, 2016 (43:10-46:24; 117:6-199:16).

g. Bard did neither before marketing Recovery Filter in the U.S.

98. Not reported in Dr. Asch's study was a fracture of the Recovery Filter which occurred in patient number 33 (one patient after the original Asch series of 32 patients). (Deposition of Murray Asch, M.D., May 2, 2016). The patient was a 29 year old pregnant female with swollen left lower extremity from deep venous thrombosis (32 weeks gestation). The patient was a high-risk OB case (breech presentation with planned C-section). She was treated with LMW heparin until 37 weeks when a RNF was inserted via right femoral approach. The patient

had a spontaneous conversion to vertex presentation one week later and she had a normal vaginal delivery. The abdominal radiograph showed a 1.5 cm caudal migration of the filter. Four weeks after delivery a routine abdominal radiograph presented one filter arm projecting above the filter, suggesting a fracture. The fracture was confirmed on a pre-removal CT scan. The filter was removed 75 days post-insertion. At the time of removal, the fractured arm was retrieved; but one hook leg had broken off and could not be identified despite imaging. Details of this case were later published in Cheung MC, Asch MR, Gandhi S, Kingdom JCP, *Temporary inferior vena cava filter use in pregnancy*. J Thromb Haemost 2005; 3:2096-7).

99. Dr. Robert Ritchie's report provides further context to the significance of patient #33. *See* Dr. Robert Ritchie's Report, *Assessment of the Bard IVC Recovery Filter Failures* (2015), pg. 18. In July 2002, a RNF Failure Investigation Report (ETR-02-06-02) authored by Doug Uelmen, Bard's VP for Quality Assurance contained the failure analysis by Robert Carr, the Program Director of Vena Cava Filters, identifying the fractured arm and foot of the filter in patient #33. (BPV-17-01-00052601). Dr. Ritchie emphasizes that processing marks associated with the centerless grinding of legs could be a substantial contributing cause of fractures, however, the Bard engineers concluded that these "defects" would not cause fracture despite the fact that one fractured arm and one fractured and missing foot had occurred. Despite such evidence of these defects, Carr concluded "[n]o processing issues were identified. No obvious flaws or defects were observed that would have predisposed the filter to the failures observed".

100. As it turned out, this filter exposed most of the defective characteristics subsequently observed in the Recovery, G2, and Eclipse Filters; and by 2002, before Recovery, G2 and Eclipse filters were released for sale to the public, Bard was in possession of substantial information indicating the failures were attributed to the filter design.

101. The same rules that form the foundation for patient safety, the safety and effectiveness of new and experimental medical products, informed consent, and periodic monitoring mandated in pilot studies and clinical trials, should be applied here; especially if the event deals with potentially fatal, unexpected and unintended complications as were revealed in the small pilot study of Dr. Asch.

102. As discussed, below, and in greater detail in the expert report of Dr. David Kessler, former commissioner of FDA, even before the clinical data, design failures and adverse events and complications that were revealed in the Dr. Asch study, the Recovery Filter failed to pass stability/migration bench testing had the threshold for pass/fail been appropriately used. The results and rationale for this pre-clinical testing should have been provided to Dr. Asch and the IRB responsible to ensure informed consent and proper monitoring of patients before the study commenced. This would have put Dr. Asch, the IRB, and clinical trial subjects on notice that the test device, the Recovery Filter, had already shown a propensity for instability and migration in the laboratory, and that no design changes were made to the Recovery Filter to deal with these test failures prior to the pilot study. (Expert Report of David A. Kessler M.D., dated September 26, 2010).

103. In Dr. Asch's May 2, 2016 deposition, he emphasizes that his study specifically focused on safety of retrievability while also studying filter performance and complications during the expected short-term indwell time of the Recovery Filter. A long-term study of the Recovery filter, he recognized was important and necessary, and needed to be structured in a different manner than the study he conducted; that is a study with a substantially larger patient population (a hundred or even a thousand) to study the safety of the Recovery Filter rather than a small retrieval study. Bard even informed Dr. Asch that they planned to perform such a study

before deciding to launch this new IVCF, and before they submitted the Recovery Filter 510(k) application for clearance by the FDA. (Deposition of Murray Asch, M.D., May 2, 2016, 19:2 - 20:17).

104. In his deposition, Dr. Asch testified that the migration of the Recovery Filter was a very dangerous problem, if a migration were to occur and if the filter or parts of the filter were to travel to the heart or lungs, it could be lethal. Dr. Asch was able to retrieve Patient #33's filter, but only one of two fractured arms, despite using imaging with a CT scanner. The patient was asymptomatic; however, he recognized that a fractured filter fragment could be lethal. He estimated the fragment sizes at 1 inch pieces. These are sharp, solid metallic objects that can act like a needle. In the particular case of the filter fracture, the filter fracture was identified 75 days after insertion (April 2002). At this point, the Recovery Filter study had been submitted to Radiology for review and this important complication was not reported in the literature until 2005. (Deposition of Murray Asch, M.D. 36:7-39, May 2, 2016); Cheung MC, Asch MR, Gandhi S, Kingdom JCP. *Temporary inferior vena caval filter use in pregnancy,* J Thromb Haemost 2005; 3:2096-7).

105. Dr. Asch testified that NMT/Bard was promptly notified about this complication and he believed an analysis had been undertaken to study this anomaly, and effectual changes related to design and robustness of the filter (increased diameter metal) were planned to prevent future fractures. The basis for resuming the trial was centered on Dr. Asch's expectation that NMT/Bard would create a new filter design and perform a long-term study on the functional parameters of the new filter. (Deposition of Murray Asch, M.D., pgs. 40-41)

106. Despite Dr. Asch's belief, in June 2002, NMT/Bard used his study to justify launching the Recovery Filter for widespread U.S. marketing and obtained 510(k) FDA

clearance based on Dr. Asch's Recovery Filter paper from Radiology, and comparing the device to the Bard SNF, Meditech (Boston/Scientific), and Titanium Greenfield as predicate devices. Dr. Asch expressed his concern to NMT/Bard that the release of the Recovery Filter should not be effective until a clinical study for safety and efficacy, not solely retrievabilty, was completed. Again, he was reassured that NMT/Bard would perform a large multicenter prospective American study to assess long-term performance of the Recovery Filter.

107. Dr. Asch submitted a letter to the Editor (2005) to the International Society on Thrombosis and Haemostasis:

a. Temporary inferior vena caval filter use in pregnancy (Cheung MC, et al). The patient described was 29 year old gravida 2, para 1 with 32 week gestation and painful left leg swelling.

b. Ultrasound showed occlusive thrombus of the left iliac vein. Dalteparin was administered.

c. Repeat U/S at 36 weeks gestation age showed distal extension of the thrombus with extensive common femoral occlusive thrombus despite anticoagulation. The patient was transferred to Sinai Hospital at 37 weeks gestation and ultrasound showing breech presentation and a C-Section was planned.

d. In view of the high risk of PE at the time of C-Section, a RNF was inserted into an infra-renal location via the right femoral vein. One week later the fetus spontaneously converted to vertex presentation. The patient was induced at 38 weeks with temporary cessation of the LMW heparin. She had a normal vaginal delivery.

e. Abdominal radiography showed caudal migration of the filter of 1.5 cm. Four weeks post-delivery an abdominal radiograph demonstrated one filter arm to be projecting above the filter, suggesting a fracture. A CT scan demonstrated the fracture and no thrombus was seen.

f. The filter was removed 75 days after implantation and the broken arm retrieved also. One leg hook had broken off as well, and CT imaging on several occasions failed to identify this tiny fragment and the patient has remained asymptomatic. It states that this is the only fracture in the Institutions (Mt Sinai, Toronto, ON) series of 58 filters. The patient in follow-up for 18 months after filter removal has remained asymptomatic. Note the following from Bard internal documents:

i. "While no true *in vivo* testing has been conducted to characterize the fatigue properties of the SNF, NMT has over 9 years of *in vivo* experience with the SNF. NMT has reviewed their clinical trial database, post-marketing complaint files and the literature to identify any fatigue related issues with the SNF. There were 2 reports pf asymptomatic filter fracture identified for a rate of 0.006% (McCowen, 1992). NMT has concluded that fatigue of the SNF has not been clinical problem."
(Line Extension to SNF/Straightline Systems, Technical File, July 17, 1997 BPVE-01-00277852 at pg. 17)

ii. "Today I reviewed all detachments reported as complaint for our Simon Nitinol Vena Cava Filter (SNF). Our electronic database goes back to 200. There were just 2 reports of fractures/detachments out of the 67,800 global sold during this time frame."
(June 10, 2004 email from Cindi Walcott, Quality Assurance, to Dr. David Ciavarella, Medical Director, BPVE-01-00509497)

g. In this paper, Dr. Asch recommended routine abdominal radiology for all filter patients in order to identify filter fracture/migration. This was never mentioned in the IFU for the RNF. The discovery of these fractures resulted in a discontinuation of Dr. Asch's pilot study. Moreover, the root cause of these fractures, like the migration in the same study, was never determined. (Cheung MC, Asch MR, Gandhi S, Kingdom JCP. *Temporary inferior vena caval filter use in pregnancy*, J Thromb Haemost 2005; 3:2096-7).

108. Therefore, in the above noted complications in 33 patients, two fractures must be added. In summary, in 33 cases, there were two (2) tilts >15° (6%), one four (4) centimeter cephalad migration with clot (3%), one (1) asymptomatic perforation (3%), and two (2) fracture fragments (one filter so 3-6%). Total complication rate was 15-18% and the average indwell time for Dr. Asch's study was 53 days with the longest indwell time was 134 days.

109. In our opinion, Bard should have halted all efforts to push the Recovery to market while a thorough investigation, further testing, and appropriate design changes were completed that assured these same events would not occur in the future under all reasonably foreseeable uses and human conditions, particularly for situations where extensive indwell periods might occur with the RNF.

110. It is further our opinion that based on the limited data from the Asch study regarding retrievability, with a mean time period 53 days, Bard should not have represented that the Recovery Filter could be safely and percutaneously removed without any indwell time limitations, or safely and effectively stay implanted permanently over the life of a patient. Such time spans could include several decades of an indwelling filter. (BPVE-01-00373887).

111. Bard's own documents indicate that its engineers did not consider the pressures, volume changes, distensibility and changing dynamics of the vena cava in testing and designing the Recovery Filter. In our opinion, explaining away the two fractures in patient #33 as pregnancy-related was speculative, as proven by the poor clinical performance and serious complications the Recovery Filter experienced very shortly after its full market release.

112. The most concerning factor to us is the rapidity with which complications were occurring suggesting the possibility that more complications might be forthcoming. While complications are often mentioned as a percentage of all filter insertions, it is best to present data such as perforation, migration, fractures, recurrent pulmonary embolism, caval thrombosis, recurrent DVT as life-table data, i.e. a rate per person per time. For example, the SNF data listed above was a 10-year study period with two documented fractures with over 67,000 SNF sold. In Dr. Asch's study two fractures in 33 patients occurred by a mean follow-up of 53 days of indwell (range 5-134 days).

V. CONCERNS ABOUT LACK OF SUFFICENT DATA USED TO SUPPORT MARKET LAUNCH OF RECOVERY FILTER AND 510(k) APPLICATION (I.E., PRE-MARKETING AND PRE-CLINICAL TESTING)

113. The Recovery Filter (RNF) is a modified Simon Nitinol Filter (SNF) with two levels of filtration. The original "daisy wheel" design with seven (7) upper loops or pedals has

been truncated with only six (6) upper truncated arms. There are six (6) lower legs with rounded hooks to engage the caval wall. The thickness of the wire for the Simon Nitinol was 0.014 inch while that of the RNF was 0.013 inches. The diameters are also different (i.e., the lateral dimensions of the upper and lower aspects of the RNF and SNF) (RNF Diagram, BPVE-01-01059087; Kessler Schedule 4).

	SNF	**RNF**
Diameter Upper	28-32mm	28-33mm
Diameter Lower	32-40mm	30-34mm

114. Moreover, there are important changes in the hooks between the two devices.

Thickness of Hook	0.014 inches	0.0085 inches

115. Review of the mechanical drawings of the hook detail on the SNF and Recovery Filter implies to us that the SNF hook has a more acute upper (cephalad angulation) while the Recovery Filter has a distinctly rounded hook shape. The smaller size diameter of the lower filter in the Recovery Filter would imply less radial force for the hook to engage the caval wall. This implies that the designers were more concerned with ability to retrieve without damage to the caval wall, but potentially at the compromise of lower thresholds for migration, embolization, and perhaps, also perforation.

116. Review of the data that preceded Bard's decision to market the Recovery Filter and the same data submitted for the FDA 510(k) application as outlined in Dr. Kessler's report and references reveal the following about migration testing:

[redacted]

117. Discussion ensued regarding the appropriate pressure threshold to be used and Dr.'s Kaufman and Venbrux were consulted. They reported that caval pressure gradients of 35 mmHg have been documented and using an approximately 50% safety margin of 15 mmg Hg; the conclusion was to use the 50mmHg limit rather than an earlier requirement of 70 mmHg; the decision was based on information from the consultants and because the in vitro testing failed the initial stated standard of 70 mm Hg. (BPV-TRIAL-EXHIBIT-0970). The 35 mm Hg pressure gradient can be found in more chronically occluded cavae which often develop collateral pathways. This static pressure also does not include transient increases in caval pressure that may occur more acutely say with Valsalva or acute embolic insult of the filter. The pressure gradient is one variable of a very complex multi-dimensional dynamic system (caval dynamics-see below) and given the low migration resistance seen with larger cavae (≥28 mm) the safety margin to prevent migration was seriously underestimated in the assumption and by the means of the in-vitro study done.

118. In our opinion, the model is exceedingly simplistic and demonstrates a flawed evaluation of caval dynamics. Venous structures provide storage for large volumes of blood at low pressures. Veins are analogous to capacitors in electronic circuits which can store electrical charges and then discharge them rapidly to support a stable voltage. The analogy in hydraulics is an accumulator, which can store large volumes of hydrologic fluid which can be rapidly delivered at fast flow rates to maintain a relatively constant pressure. The pressure test for migration measures one parameter (pressure gradient) in what is essentially a multidimensional (multifunctional) process- normal changes in caval dimensions with normal activities of life are ignored. There are dynamic respiratory and cardiovascular changes which can be reflected in caval dynamics (changes in caval size). In patients with tricuspid valvular incompetence and pulmonary hypertension changes are readily seen on cavography with reflux of contrast material into the hepatic and renal veins clearly influencing the diameter in the cava. More semi-static changes in caval dimensions can reflect fluid status of the patient, as well.

119. We, as interventional radiologists, may see a flat cava on CT imaging of a trauma patient in shock as a result of multi-organ injury. Moreover, in the end-stage renal disease patient who is fluid overloaded and in need of dialysis, the CT abdomen will show a distended round cava compared to the usual ellipsoid appearance of the IVC on cross-sectional imaging. The concern is that the addition of the supporting plastic tube over the casing is not a representative in-vitro situation for testing migration of the retrievable versions of the Bard filters. It is possible to imagine a situation, say a sudden Valsalva maneuver, where the caval dimensions exceed the dimension of cava for which the RNF was indicated for (28 mm). Could such a distended cava cause hook fixation to fail? It would seem this might be possible even without occurrence of filter fractures or embolic (clot) insults.

120. Another factor is the safety concerns related to the pressure gradient test. The initial 35 mmHg gradient threshold had a 15 mmHg safety margin, which represent a 42% safety factor. Concerns include the risk of filter migration, such as migration to the heart or pulmonary circulation with possible risk of injury to those organs, including death. Another concern is the obviously loss of protection from PE, which may go un-noticed. Retrieval of migrated filters to cardiac and pulmonary structures requires advanced retrieval techniques and added risks of complications well beyond those associated with caval retrievals. Given these concerns, Bard should have used higher safety margins. Common safety factors used in engineering are as follows:

Equipment	**Factor of Safety**
Aircraft Components	1.5-2.5
Boilers	3.5-6
Bolts	8.5
Engine Components	6-8
Rotating Turbine Components	2-3
Wire Ropes	8-9

(For example, http://www.engineeringtoolbox.com/factors-safety-fos-d_1624.html)

121. Generally, and of interest here, lower safety factors are employed only when well-known or classified materials and conditions of loading are well specified, while higher factors are used with uncertain materials and loading conditions.

122. In our opinion, IVC filter falls into the latter category. As discussed, below, there was no safety factor built into the tests run by Bard on the Recovery Filter. On the contrary, based on animal data, even without a safety factor, the minimum migration threshold should

[redacted]

123. [redacted]

124. Bard's 510(k) application for the Recovery Filter device did not disclose that filters at the lower end of the leg span set specification met the migration resistance test when their hooks were engaged, but that those hooks were not always engaged. (BPV-17-01-

00057953-8037; Kessler Report pg. 39, para 93). Moreover, Bard's IFU makes no mention of the need for physicians to assure the hooks are engaged, or that the device failed the migration resistance testing when hooks were not engaged. (BPVE-01-00435559-592; Kessler Report, pg. 39, para 94).

125. [redacted]

126. Accordingly, we, as potential customers and consultants to Bard, and as policy and guidance authors for the SIR, and as physicians with patients looking to us for appropriate health and treatment advice, expect that with these additional pre-clinical test results, coupled with the scant, yet troubling, clinical data that Bard would recall the Recovery Filter from the open market.

127. [redacted]

128. [redacted]

129. [redacted]

[redacted]

130. [redacted]

131. [redacted]

[redacted]

132. [redacted]

[redacted]

[redacted]

133. [redacted]

134. Dr. Ritchie performed an extensive analysis of twelve (12) retrieved fractured RNF's and an analysis of two (2) expired and two unused (exemplar) RNF's to evaluate initial

surface conditions of the devices prior to implantation to assess surface conditions on filters not related to handling, insertion, and retrieval. The twelve (12) retrieved, fractured filters revealed:

a. All filters showed evidence of fractured arms and legs. The arms (typically two-three fractures per device) failed at or just below the filter sleeve. The legs (typically one-two per device) failed in the feet along the concave surface of the anchoring hook. Specifically, approximately 44% of the arms and approximately 28% of the legs were found fractured on the explanted devices.

b. All fractures resulted from cyclic fatigue failure involving fatigue cracks that initiated on the surface of the wire arms (and legs) and propagated some 33% to 50% into the cross-section before the wire completely fractured due to ductile overload fracture.

c. The nature of the surface of wire arms and legs was microscopically rough, involving circumferential grinding marks on the tapered portion of the legs and more importantly draw marks, pock-marks and some circumferential markings on the surface of arms. There was additional evidence of more serious gouge marks in the bend on the arm surfaces. Such surface damage was seen on the "exemplar" filters too. The presence of such manufacturing defects on these components, which could have readily been removed by electropolishing (or in the case of the gouges avoided by improved manufacturing procedures and/or quality control), significantly raised the likelihood of fatigue fracture crack initiation and device failure in vivo. [He makes the important observation that effect of electropolishing Nitinol was known in the mid-1990's for wire stents (arterial) and clearly established that the reduction in surface roughness from electropolishing reduced susceptibility to fatigue failure and further promoted the corrosion resistance of Nitinol wire.] Nitinol Devices and Components (NDC) was selling their Smart Stent in 1998 which was an all electropolished Nitinol medical device. Again, this implies the design engineers underestimated the loading stresses placed upon the RNF in vivo. The later versions of the Bard Filter did eventually utilize electropolishing establishing this as an important manufacturing change to reduce fracturing.

d. Many of the wire arms that suffered fatigue failures fractured where the wires emerged from the filter sleeve. There is clear evidence of the location of the initiation of these cracks were the wire contacts the edge of the inner-diameter rim of the cap or filter top. There are high bending moments at

these locations. The baseline stresses on the arms is magnified several-fold by stress concentration factors which occur by the sharp edge of this inner rim where it contacts the arm. The design diagrams specified a chamfered (or radius of curvature) for this inner margin of the sleeve which when examined did not achieve the called-out specification. Ritchie makes an important point that the Simon Nitinol filter had a 45° chamfer and engineering drawings (2002) of the recovery under the Bard name, also required this chamfer which was not achieved with the RNF. BPVE-01-00012778. Dr. Ritchie on his analysis measured the chamfer of about 10 цm (Ritchie; -"extremely sharp corners"). Bard in subsequent design versions- the G2 express display the 45° chamfer on the inner edge of the sleeve rim as design features to reduce apparent stress conditions at this location.

e. Other arm fractures occurred just below the sleeve at or near the first bend in the wire. Dr. Ritchie found surface gouges at this location, which he felt were from the manufacturing process of shaping the curves on the arm.

f. The rough circumferential centerless grinding markings at the "ankle/foot" region of the filter legs, which Bard could have electropolished provided severe stress concentrations in those areas with fatigue failures in those locations. The clear majority of the fracture legs examined by Dr. Ritchie occurred in these locations. As indicated above, in comparison to the Simon Nitinol the hook is reduced in wire diameter (by this grinding) reducing its strength compared to the Simon Nitinol filter. The grinding process produces surface abnormalities which were left which caused stress concentrations so may have predisposed these areas of the hooks to failure. Once one hook failure occurs, more stress is placed on the remaining hooks exposing those filter legs to additional possible failures, less force for fixation, and more opportunity to migrate and embolize. Also, there is less ability to sustain the retaining forces needed to stop an embolism of thrombus. Additionally, loss of arms or legs is loss of filtering elements so less effective clot trapping. Dr. Robert Ritchie Report, pgs.33-35, March 3, 2017.

135. In our opinion, filtering for clots within the cava is essentially a geometric issue, as the gaps present in the cross-section of the filter between adjacent arms or legs allow clots to pass through. Loss of a filter element such as an arm or leg, results in larger gaps and can allow more and larger clots to pass. This ignores the increased loading conditions the loss of a filter arm or leg places upon the remaining arms or legs.

136. [redacted]

137. [redacted]

138. Clearly these design issues related to migration and fracture of the Recovery Filter. The RNF brokered new, unknown ground in regards to retrievability. In our opinion, the design focused too much on making features to facilitate ease of retrieval (i.e. low forces)-

smaller wire sizes, ground-down hooks, smaller diameters in the upper and lower filtering segments, rounded hook design in RNF compared to Simon Nitinol, and also lower number of elements (7 arches in upper filter element of Simon Nitinol versus 6 in RNF). But, ease of retrieval has a design tradeoff- ease of migration and possible embolization. The reduction in wire sizes, manufacturing issues and uncertain loading conditions created potential physical stresses on the filters or parts of filters perhaps pre-disposing filters to fracturing, migrating, tilting, perforating and embolizing with serious potential consequences. Filters with loss of components even greater stresses, exposing them to greater loads and compromised filtered efficacy as mentioned above.

139. In our opinion, and consistent with Dr. Kinney's advice to Bard as a consultant, the expectations of members of SIR, and other physicians who order and implant IVC filters from the standpoint of stability and strength, safety and effectiveness, risk and benefit, should not be compromised in making an IVC filter retrievable, especially if the device was also indicated for permanent placement. As Rob Carr, Vice President of Engineering, stated in his deposition (April 17, 2013, page 32, lines 10-23) our retrieval devices are first and foremost permanent devices.

140. Moreover, Bard represented and marketed their devices as new, improved and taking strength and stability to a new level. Never was there a communication from Bard, nor was any data of internal analyses shared with physicians which would indicate any Bard IVC filter had design defects or features that statistically significantly increased the risk of known potential complications, including the very rare risk of death from embolization of the entire filter when challenged by clot(s), perforations, thrombi or the embolization of broken pieces of metal to other organs.

VI. BARD LEARNED OF DESIGN FAILURES THROUGH DEVELOPMENT AND TESTING AND DID NOT NOTIFY PHYSICIANS OF THEIR DEVICE'S DEFICIENCIES

141. The full market release of the Recovery Filter in the U.S. took place in January 2004.

142. From March 24 - 30, 2004, the annual Society of Interventional Radiology (SIR) Meeting was held in Phoenix Arizona. Dr. Kinney moderated a session IVC filters including retrievable filters with much enthusiasm raised about the ability to retrieve filters at a much longer filter in-dwell time compared to the Gunther Tulip or temporary filters alluded to above. The newer filters could be removed when the risk of DVT/PE had resolved and/or the patient had recovered completely. At the conference, Dr. Kinney raised a concern that ease of retrievability might also result in higher rates of migration than was seen with the more extensive experience with permanent filters. Shortly after the session presented by Dr. Kinney, Bard hosted an animal training session to train physicians on insertion and retrieval of the Recovery Filter; of note, Bard did not share any of its findings on the Recovery Filters design defects.

143. A former Interventional Radiology fellow at UCSD, Dr. Alex Powell, experienced a fatal migration of a RNF in an obese patient, within weeks after the March 2004 SIR meeting. The filter had been in place a relatively short period of time and the patient went into the bathroom to relieve himself and died. The assessment was embolic insult of the RNF in an obese patient.

144. However, prior to Dr. Powell's experience, [redacted]

[redacted]

145. On April 14, 2004, Bard received a second complaint from the field about a migration of the Recovery Filter and patient death.

146. [redacted]

[redacted]

147. [redacted]

148. [redacted]

149. [redacted]

150. [redacted]

151. [redacted]

152. [redacted]

[redacted]

153. [redacted]

154. [redacted]

A. G2 Testing Concerns

155. Bard made design changes in developing the Modified Recovery (G2). A Bard

Document titled "G1A Filter and Femoral Delivery System-Consideration for Development of Design Testing Requirements," under the heading "Summary of Design Changes," noted:

[redacted]

156. [redacted]

[redacted]

157. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

158. [redacted]

[redacted]

159. [redacted]

160. [redacted]

B. Caudal Push Migration Test

161. [redacted]

162. Inferior migration of vena cava filters had been previously seen and reported with the release of the Titanium Greenfield IVC filter which had upwards of a 20-30% inferior migration rate. Greenfield LJ, et al. *Results of a multicenter study of the modified hook-titanium Greenfield filter*. J Vasc Surg 1991; 14(3):253-7. The Boston Scientific/Meditech engineering staff came out with a modified hook design. In this configuration, a minority of hooks (2 of the

6) were directed to oppose inferior or caudal migration while the majority of hooks were oriented to prevent superior or cranial migration. This hook design element was recognized and reported in 1991. The later generations of the RNF/G2, the Denali (cleared in 2013) finally utilized such hook modifications to ameliorate the caudal migration found with the G2.

C. <u>Modified Recovery (G2) Corrosion Resistance Testing</u>

163. [redacted]

164. [redacted]

[redacted]

D. G2 Post-Market Experience

165. [redacted]

166. [redacted]

[redacted]

E. [redacted]

167. [redacted]

[redacted]

[redacted]

168. [redacted]

F. <u>Filter Expert Panel Meeting Chicago on June 1, 2006</u>

169. Dr. Kinney attended this meeting and was asked about the expected rates of performance data of IVC filters such as recurrent PE rates and complications such as perforation,

fractures, death, and migration (> 2 cm). He believes recurrent PE rates with filters should be at least as good as anticoagulation therapy (2-5%). Minimal IVC perforation was recognized as a known complication and often of no clinical significance; however, there was concern if the design of the filter was such that it would increase the potential for deeper perforations that would "compromise" structures such as aorta, visceral organs (kidney, pancreas. liver) or bowel.

170. Unanimous consensus was present that fractures and filter related deaths should be as close to 0 % as possible. Fracture with embolization of the fragment or filter were recognized as serious, potentially life-threatening concerns. None of the historical data and events, referenced above, that predated this meeting were shared during the meeting.

G. Bard's successor to the G2/G2X was the Eclipse Filter

171. As stated above, within 2-3 months after the launch of the Modified Recovery (G2) device, Bard learned of design issues with that device from increasing problems with tilt, fracture, migration and perforation (e.g., February 2006 HHE). These discussions continued without any affirmative action by Bard to advise physicians and patients, and instead of removing the device from the market Bard continued to actively market and sell this device without a new iteration until the launch of Eclipse approximately five years later.

172. In 2008, at about the two and half (2-1/2) year mark of this five year period, Bard had a meeting "to analyze EVEREST and MAUDE data and provide justifications for proposed changes to G2 filter," and "The new improved filter platform (G2 Platinum)." Slide 3 of the presentation states:

[redacted]

173. [redacted]

174. [redacted]

175. [redacted]

[redacted]

176. [redacted]

177. [redacted]

178. [redacted]

[redacted]

179. [redacted]

180. [redacted]

181. [redacted]

[redacted]

[redacted]

182. In our opinion, the Eclipse did not incorporate the necessary design or other fixes to resolve the short and long history of unacceptable complications and risks associated with the G2/G2X filters, and like the Recovery, G2 and G2X iterations of Bard's IVC Filters, it should have not been marketed by Bard as designed and represented. Once having made the decision to launch and sell the Eclipse in the open market, the reasonable expectations of physicians and members of SIR, and others who order and/or implant these devices should have been provided these details, facts and statistical analyses set forth within Bard's internal documentation. Had we and other reasonable physicians been privy to this information it is more likely than not we would have not used this device, and at a minimum we would have shared this relevant information with our patients, members, colleagues and other physicians.

VII. IMPORTANT ARTICLES DISCUSSING COMPLICATIONS WITH IVC FILTERS

183. The early signals, data and questions regarding the strength and stability of marketed designs and false and misleading claims of the safety, performance, quality and effectiveness of Bard's Recovery, G2/G2X and Eclipse Filters, as Bard should have expected, became the subject of several peer-reviewed articles in the medical literature. These articles are referenced in our "Facts and Data Considered" Schedule. The findings within these studies were predictable from both the pre-clinical and clinical data, as well as adverse event comparative analyses. A sampling of these articles follows.

184. In 2006, the year after Recovery was removed from the market, Dr. Kalva and colleagues, in an article published in Cardiovascular Interventional Radiology, titled "Recovery Vena Cava Filter: Experience in 96 patients," reported that of the forty (40) patients who had abdominal CT at a mean of 80 days, there were high rates of adverse events: The filter arms penetrated the IVC wall in 11 (27.5%) of patients. In three (3) of the eleven (11) patients (3/40, 7.5%), the arms were fractured (or acutely bent). In one patient, the fractured arm migrated to the pancreas. In the other two patients, the fractured arms were attached to the main device protruding in to the aortocaval space. In 5 of the 11 patients, the filter arms were seen protruding in to other organs such as the duodenum (4 patients) and liver (one patient). Given these, the authors suspected structural weakness in the filter.

185. In 2008, Oliva et al. published a retrievability study of 120 Canadian patients with the G2 filter. Among these 51 of the 120 patients who had filter removal - 12% had filter tilting (>15%); 18% had IVC penetration; and 3.9% had caudal migration. (Oliva VL, Perreault P, Giroux MF, et al. *Recovery G2 inferior vena cava filter: technical success and safety of retrieval*. J Vasc Interv Radiol 2008: 19: 884-89).

186. In 2009, Hull, et al, published the results of a retrospective evaluation of 14 patients who received the Recovery filter. At long term follow-up (mean 899 days), all 14 patients had filter arm perforations; 36% had leg perforations; and 21% had fractures associated with migration. The authors concluded that Recovery filter limb perforation increases over time and is associated with a 21% incidence of filter arm fracture and migration. The authors recommended follow up imaging for patients receiving these filters. (Hull JE, Robertson SW. *Bard Recovery filter: evaluation and management of vena cava limb perforation, fracture, and migration.* J Vasc Interv Radiol 2009; 20:52-60)

187. In 2010, Nazzal, et al. published a retrospective review of 400 filters placed at their institution. 34 were Recovery filters and 5 were SNF. The authors reported that 2.9% of the patients with Recovery filters had post-insertion DVT, while 8.8% had caval thrombosis and 11.8% had migration/tilt. The authors noted that "the incidence of tilt/migration was the highest in the Bard RNF filters (11.8%) compared to each of the other filters (p<0.004) or to all other filters collectively (p<0.0005)."

188. In 2009, Binkert, et al, reported on a prospective, multi-institutional study (11 sites) of the technical success and safety of the G2 filter. One hundred patients with a temporary indication for caval interruption were enrolled in the study from Dec 2005 until July 2006. Radiographs were obtained AP, Lateral, and bilateral oblique's within 48 hours of filter placements. There were 67 men and 37 females with a mean age of 52.1 years (range, 19-82 years). More than half of the patients had trauma as an indication for filter insertion and 16 % were having surgery within one month of filter placement.

Forty-two patients had VTE- 18 with DVT only, 10 had PE only, and 14 both PE and DVT. The Primary objective was to assess technical and clinical success of G2 retrieval including adverse events within 30 days after retrieval. Filter migration (defined as > 2 cm was documented on plain radiography or venography). Fractures were defined as loss of integrity of separation while perforations were defined as > 3mm outside of the cava on venography. The results showed two filters tilted more than 15 degrees after placement. At study completion 83 of the 100 patients enrolled had a complete data set. Retrieval was attempted in 61 patients with 3 failures due to embedded filter tip in the caval wall. The mean indwell time for filters was 138 days (range, 5-300 days). There were two symptomatic PE's with filters in place. Migration of >2 cm occurred in 10 of 85 patients (12%) at a mean follow-up of 155 days (range, 5-323 days),

but it is worth noting that there were about double that number for migrations (in both directions) between 1 and 2cm. The mean migration distance was 2.7 cm (range, 2-4.1 cm). All migrations (>2cm) were caudal. One filter fracture occurred in the 85 assessed devices (1.2%). Filter tilt increased with time with 15 of 85 (15%) tilting more than 15 degrees. It is worth noting that a tilt of approximately 20 degrees places the apex against the inner lumen of the vena cava and the risk of endothelialization with resultant difficulty to remove, percutaneously/intravascularly. Filter penetration assessments were only possible on 61 patients, but 16 of 61 patients (26%) showed a filter leg or arm penetrated more than 3 mm outside the IVC. Fifteen of the 16 penetrations were asymptomatic; one patient reported back pain relieved after filter retrieval. Filter tilt of more than 15 degrees and migration were significantly associated. Binkert, et al. "*Technical Success and Safety of Retrival of the G2 in a Prospective, Multicenter Study*," JVIR 2009; 20:1449-1453.

189. Also in 2009, Lynch and Kekulawela published a retrospective analysis of 174 filter removals involving the G2. (Lynch, MD and Stephanie Kekulawela, MD, *Removal of the G2 Filter: Differences between Implantation Times Greater and Less than 180 Days*, J Vasc Interv Radiol 2009; 20:1200–1209). IVC penetration was found in 44%, fracture in 3.4%, migration in 52% (12% had migration greater than 20 mm).

190. In 2010, Nicholson, et al, sought to determine the prevalence of fractures and embolization of the Bard Recovery and G2 filters. They conducted a retrospective, single-center, cross-sectional study evaluating all patients who received either a Bard Recovery or G2 filter from April 2004 until January 2009. A total of 189 patients had undergone implantation-but 1 pregnant patient and 35 patients who died were excluded in addition to 10 patients who had filters removed. So ultimately, 80 patients participated in the trial (many patients could not be

found for follow-up). Subjects underwent fluoroscopy to assess filter integrity. Embolized fragments were localized by fluoroscopy and echocardiography and cardiac CT performed if fragment embolization to the heart was suspected. Thirteen of the 80 patients (16%) had 1 strut fracture. At least 1 strut in 7 of the 28 Bard Recovery filters fractured and embolized (25%). In 5 of these 7 cases, patients had at least 1 fragment embolized to the heart (right ventricle) (71%). Three patients had life-threatening symptoms of ventricular tachycardia and/or tamponade, including one patient who experienced sudden death at home. Six of 52 G2 filters fractured (12%). In 2 of these 6 cases, the patients had symptomatic end-organ fragment embolization. Since the duration of follow up for the G2 was less than with the RNF, the authors hypothesized that the fracture rates of the two filters may actually be similar. They submitted a correction later concerning number of patients but felt the outcomes were still valid. They felt that patients and physicians should be notified about these potentially life-threatening complications.

191. The results of the Nicholson study are especially concerning with unacceptably high rates of filter fracture and migrations with both the RNF and G2 implying that the issues that had presented early with the RNF had persisted and accumulated after the introduction of the G2 in 2005. The filters that fractured had a high proportion of fragments that embolized to the heart with possible life-threatening complications. Although, the fractures appeared about half as prevalent in the G2 as compared to the RNF, the follow-up period was shorter for the G2 and the rate may ultimately be comparable. (Nicholson, et al. "*Prevalence of Fracture and Fragment Embolization of Bard Retrievable Vena Cava Filters and Clinical Implications Including Cardiac Perforation and Tamponade*," Arch Intern Med 2010; 170(20); 1827-1831.)

192. In 2011, Stavropoulos, Oh, et al, [*Removal of Retrievable Inferior Vena Cava Filters with Computed Tomography Findings Indicating Tenting or Penetration of the ICV Wall*

J. Vase. Interv. Radial. (2011) 22: 70-74] found that Bard’s Recovery and G2 filters in their cohort represented the vast majority of perforations, including engagement of adjacent organ structures. The reported filter Fracture rate was 12.5%).

193. Also, in 2011, Angel, et al, reported that the Bard G2 filter represented 84% of all reports of IVC filter fracture to the United States FDA, and, that the Bard G2 filter was responsible for 59% of all reports of adverse events to FDA concerning IVC filters, 68% of all reports of perforations of tissue to FDA concerning IVC filters, 68% of all migrations of IVC filters reported to FDA, 83.5% of all fractures of IVC filters reported to FDA and 32% of all "other" reports of adverse events to FDA concerning IVC filters). (*Systematic Review of the Use of Retrievable Inferior Vena Cava Filters,* J. Vase. Interv. Radiol. (2011) 22: 1522-1530).

194. In 2012, Tam et al. published the results of a retrospective study of 363 patients who received Recovery filters at the Cleveland Clinic Follow-up imaging revealed 26 limb fractures in 20 patients; 8 fragment migrations into pulmonary arteries; 7 into iliac/femoral veins; 1 into the right ventricle; and 1 into the renal vein. The authors concluded that the Recovery filter is associated with an estimated 5.5 year fracture risk of 40%. (Tam MD, Spain J, Lieber M et al. *Fracture and distant migration of the Bard Recovery filter: a retrospective review of 363 implantations for potentially life-threatening complications*. J Vasc Interv Radiol 2012; 23:199-205).

195. Again, in 2012, Vijay et al. published a study comparing the Recovery and G2 filters. Among 548 patients presenting for filter retrieval, 63 had fractured filters (12%). The distal embolization rate of fractured filter components was 13%. They also found that filter fracture rates increase with longer dwell times. Fracture of filter affected successful removal of the filter components (98.4% vs. 53.4%). (Vijay K, Hughers JA, Burdette AS, et a*l. Fractured*

Bard Recovery, G2, and G2 express inferior vena cava filters: incidence, clinical consequences, and outcomes of removal attempts. J Vasc Interv Radiol 2012; 23:188-94).

196. In 2014, An, et al published a retrospective study examining 684 patients with G2 devices; 13 patients were identified with fractures. Struts were identified in the pulmonary artery, right ventricle, pericardium, iliac vein, and kidney. They estimated a 5-year fracture prevalence of 38%. (An T, Moon E, Bullen J, et al. *Prevalence and clinical consequences of fracture and fragment migration of the Bard G2 filter: imaging and clinical follow-up in 684 implantations.* J Vasc Interv Radiol. 2014;25(6):941-948).

VIII. KNOWLEDGE OF ALL PERTINENT INFORMATION IS IMPERATIVE TO A PHYSICIAN WHEN MAKING A RISK BENEFIT DETERMINATION

197. IVC filters are a controversial subject with much debate about the benefits, indications, risks of these devices. We are aware of standards for IVC filter placement from the following organizations: Society of Interventional Radiology; American College of Radiology, American Heart Association, American College of Chest Physicians, and others as well.

198. In fact, it is difficult to find randomized trials which show any mortality benefit of IVC filters in patients with thromboembolic disease. Unfortunately, the randomized trial data such as Prepic I and Prepic II compared patients on anticoagulation for their thromboembolic disease with or without addition of filters. While they can show reduced PE rates when filters are added to the anticoagulation regiment mortality benefit is not shown.

199. There is evidence from small trials that those patients who have suffered a PE and do not receive anticoagulation medications have mortality as high as 30 % if not treated. Information such as this is used to justify placement of filters in patients who have had a

pulmonary embolism and failed anticoagulation or cannot be anticoagulated, for example recent gastrointestinal or cerebral hemorrhage, or recent surgery. A small but significant minority of patients with DVT may have a PE. The benefit of an IVC filter protecting a patient with a DVT from PE is expected to be less than in patients who have experienced a PE. It is not entirely clear why this is so. We think some of this may relate to our lack of understanding of clot mechanic properties.

200. For example, some patients that develop a DVT may autolyze their clot (that is dissolve) it and about 1/3 of patients treated with anticoagulation may do this. Depending upon how this occurs the clot may dissolve without symptoms but it may also dissolve its adherence to the venous wall and embolize to the lungs. Many patients partially clear their clots and this involves clot maturation which may strengthen the clot's attachment to the venous wall. This takes time to occur, perhaps a couple of weeks. There is an implication that after a deep venous thrombosis, the risk of embolism of this clot is an early one. Clinical data also suggests that those patients who are inadequately anticoagulated early to therapeutic levels are at increased risks of embolic phenomena or extension of the DVT.

201. We stress that IVC filters do nothing to treat the deep venous thrombosis; IVC filters only protect patients from pulmonary embolism. Pharmacologic anticoagulation is the hallmark therapy for venous thromboembolism (DVT/PE) because it is effective in treating DVT.

202. When we evaluate a patient for filter placement, the indications require an assessment of risk and benefit. The benefit to the patient is protection from pulmonary embolism. The risks of placing a filter include risks of the procedure itself and long-term issues that may

arise. Insertion complications can be errors related to technique, such as placing a filter in the wrong position. This can include misplacement of filters in structures that mimic the IVC.

203. Typically, we place IVC filters in an infra-renal location but in less 10% of cases a suprarenal IVC filter placement may be needed. Veins that can fool an operator are the gonadal vein or hepatic veins (for supra-renal position). The veins can be anatomically variant; about 1% of patients may have two cavae and placing an IVC filter in one may not protect against pulmonary embolism if the deep venous thrombosis occurs in the unfiltered side.

204. About 1% of patients can have a mega-cava, which is typically defined as IVC diameters greater than 28 or 30 mm. Filters placed in a mega-cava may fall outside the IFU indications for some filters and may be more prone to filter migration/embolization. Bleeding and infection can arise in the insertion process as well. Rarely, we have seen filters misplaced in arterial structures (aorta for example) which provides no benefit for clot trapping and may serve as a source for clot to embolize into the arteries of the legs. Most IVC filters are placed with ultrasound access into the vein and fluoroscopic control to image and place the filter with a high degree of accuracy.

205. Once the filter placed other complications may occur. Filters may fracture; they may perforate the cava, and may migrate within the cava. They may thrombose the cava if too much clot is trapped within the filter and the blood flow through the cava, stagnants and clots with the IVC. There is debate whether the filter causes de-novo clot itself by being within the vena cava. Sophisticated flow models suggest alteration in blood flow which may make such thrombosis possible, particularly in patients who are predisposed to forming clots. Such patients may have a deficiency of various clotting factors which places them at risk for deep venous thrombosis and pulmonary embolism. Very rarely, patients are allergic to their filter components.

Migration has had various definitions over time, but one standard has been 2 cm. Migration may be locally, nearby in the cava but can also be further away; for example, inferiorly into an iliac vein which may leave the patient only partially protected. Superior, cranial migration can have serious complications such as cardiac arrhythmia's, cardiac perforation with potential tamponade, and embolization to the lung. Obviously, the patients with such a migrated filter are no longer protected from PE.

206. Another complication of the filter is guidewire entrapment which occurs during attempted central line placement usually in a sick patient needing ICU supportive care. The J guidewires with such central line kits may become attached to the filter which may result in the filter being pulled to anomalous locations if the wire becomes ensnared on the filter. The migration can occur when the wire is attempted to be removed.

207. An early filter was the Mobbin-Uddin (1967) but this silicon covered filter was prone to caval thrombosis as well as migration. Lazar Greenfield in the 1973 developed the Greenfield filter which was inserted via a cut down on a vein. Dr. Greenfield designed the filter in conjunction with a petroleum engineer with a conical shape that could contain or trap a clot (or embolism) while maintaining caval patency. In 1984, interventional radiologists developed a technique to insert the Greenfield percutaneously. The Greenfield has had several iterations including the titanium version and finally the over-the-wire Stainless Steel Greenfield (see reference below for this trial). Other filters came onto the market- Birds Nest Filter (for up to 40 mm cava), Vena Tech (original and low-profile), Simon Nitinol, and the Trapease. The permanent filters were studied mostly with retrospective studies but had fairly well-defined performance characteristics- including such important data as recurrent PE, caval occlusion, fractures, recurrence of DVT, and migrations. The indications for filters were fairly restrictive at

first, used for patients who had either deep venous thrombosis or pulmonary embolism but could not be anticoagulated. Gradually, expanded indications developed. Some included high-risk free-floating deep venous thrombosis, or patients' in whom it was felt they would be unable to tolerate any additional pulmonary embolism (pulmonary compromise). Some indications included placing filters prophylactically for a patient who did not yet have thromboembolism but had underlying conditions which placed them at high risk for deep venous thrombosis and possible embolism. The prototype indication for prophylaxis is the massively traumatized patient. Upwards of 40 % of such patients may develop a deep vein thrombosis and a significant minority may suffer a pulmonary embolism (sometimes fatal) during their recovery. Once the trauma patient is up and walking and their injuries have healed, it is possible that their risk of thrombosis is no worse than before their trauma. However, the practice of inserted permanent filters in these patients or any patient with transient thromboembolic risks subjected those patients to possible long-term filter complications. Data from the Prepic I study showed that filters while they reduced pulmonary embolism at 12 days and 2 years, the patients had excessive rates of deep venous thrombosis (some with caval clots) despite anticoagulation. This finding has led many physicians to feel life-long anticoagulation may be needed in any patient with a permanent filter. Admittedly, this is a controversial concept but nonetheless many practitioners believe this to be true. So the ability to remove a filter when the risk of thromboembolism was no longer present represented a significant advance in filter technology.

208. In discussing risk and benefit it seems to me that patients who have suffered a pulmonary embolism are at high risk for another embolism which may be fatal. This is best treated with pharmacologic means. When medical therapy cannot be used, the benefits of the IVC filter have a real value. In this setting it is understood that this benefit of the filter may be

partially eroded by small, but significant filter risks we mentioned above. Such a case represents a so called absolute indication for filter. A similar situation is a deep venous thrombosis patient who cannot be anticoagulated or developed a bleed on anticoagulation or extended clot on therapeutic doses of anticoagulation. The softer indications are considering relative indications such as adding a filter on top of pharmacologic therapy for patients with deep venous thrombosis. The patients considered for prophylactic filters may have the lowest risk of thromboembolic complications overall. Since these cases are expected to achieve a lesser benefit it would seem to us the tolerance for complications of the filter itself would have to be similarly reduced to keep the risk/benefit ratio in line across different indications for filters.

209. The retrievable filters were marketed in many situations for the prophylactic and relative indications with the understanding that these filters would be removed. Interestingly, Bard's justification for marketing and its representations of a new and improved device and the FDA clearance was really based upon permanent implantation assumptions. Many retrievable filters went into patients with the assumption they would be removed but many studies have documented that retrieval rates early in the experience were fairly low, as low as 10 %. The retrieval process itself has risk as well, such as bleeding, inability to retrieve the filter, perforation of the vena cava, and thrombosis of the cava.

210. Therefore, in our opinion the safety profile of a retrievable filter should exceed that of the earlier generation permanent devices since the retrievable filters were more frequently being used for the relative or prophylactic indications. It appears that the long-term performance characteristics of the retrievable filters were assumed to be similar to those of permanent filter but this belies the design changes made to ease retrieval. These changes included altered hooks,

thinner metal struts, less metal struts, and more flexible materials such as nitinol as compared to stainless steel.

IX. SIR QUALITY GUIDELINES ARE NOT ACCEPTABLE THRESHOLDS FOR MANUFACTURES

A. <u>The Applications and Limitations *Quality Improvement Guidelines*</u>

211. Society of Interventional Radiology (SIR) is a nonprofit, professional medical society representing more than 6,500 practicing interventional radiology physicians, scientists and clinical associates, including physician assistants, nurse practitioners, radiologic technologists and paramedical professionals. One of SIR's goals is to ensure high-quality outcomes and patient safety in vascular and interventional radiology. SIR's members work in a variety of settings and at different professional levels—from medical students and residents to university faculty and private practice physicians. The society's core purpose and mission is to work with its members to deliver patient-centered care through image-guided therapy.

212. The SIR Standards of Practice Committee conducted a meta-analysis of published peer-reviewed medical literature. This analysis summarizes the results found in published medical literature. The ultimate goal of the meta-analysis is to calculate a "weighted average" of the effects of interest. An in-depth literature search is performed by using electronic medical literature databases. The qualitative weight of these articles is assembled into an evidence table, which is used to write the document such that it contains evidence-based data with respect to content, rates, and thresholds.

213. A medical literature meta-analysis should neither be a replacement for well-designed large-scale randomized studies nor a justification for conducting small underpowered studies.

214. Like all studies, the methodology for a medical literature meta-analysis has several limitations. In these papers, the authors focus on providing practicing physicians with instructional guidelines for quality assessment purposes. Because of the use of the document the underlying data from the cited studies is not specifically evaluated including: observations of the varying patient populations, type of filter studied, methods of analysis, inconsistent coding of variables across studies, underreporting of adverse events, generalization and application of results, differing levels of evidence, or establish point estimates with confidence intervals.

215. **Patient populations not studied:** Due to the varying range of patient populations that qualify as candidates for IVC filter placement procedure, the SIR authors focused on their objective to provide written guidelines to be used in quality improvement programs and determined the outcome measures or indicators for complication rate for all patient populations, as evidenced in Tables 1 and 2. (Schedule 1, list of filters studied).

216. **Filter type not studied**: The SIR article does not attempt to categorize the reported rates by filter type. The 2011 SIR article explains "[f]ew comparative studies have been completed to evaluate all filters in one project, and those that have done so have been retrospective analyses. Complication rates are highly variable depending on the filter being studied." The ranges from the medical literature referenced are often very wide, and in turn the Tables represent reported outcomes from various publications and not an SIR threshold for complications (e.g. migration 0-18% and fracture 2-10% and IVC penetration 0-41%). Because there can be wide ranges between different filters, the thresholds are not meant for practitioner

reliance. For example, the suggested threshold of <1% for death is inadequate if one type of filter has a death rate of 0.9% and another has a death rate of 0.1% - a 9-fold difference. Certainly, such a difference in death rate should never be used by anyone, including IVCF device manufacturers, just because both are <1% to suggest that there are no differences in this most serious complication and that both devices are equally acceptable risks to members of SIR or any other physician who prescribes or implants these devices.

217. **Limitations based differing methodologies and outcomes of studies:** A review of the references cited in the 2003 and 2011 articles demonstrates the intent of the SIR authors to provide an abridged summary of medical literature for purposes of hospital quality assurance programs. A brief analysis of the limited filters studied, purpose for the studies and the conclusions reached. In these articles, a majority implore continued review and research based upon nascent nature of these devices during the period of study 1989 – 1998.

218. Many of the referenced medical literature relied upon in support of the SIR article recommend that manufacturers design safer and more effective devices, and encourage the medical community to continue studying these devices. Twelve (12) of fifteen (15) articles suggest the "scientific evidence for filter effectiveness is lacking" and comment on the need for long-term studies, "a national filter registry or multicenter study of IVC filters might help to resolve some of the unanswered questions regarding filter efficacy and safety. (Schedule 1, SIR Quality Improvement Guidelines: Analysis of filters studied, outcome and conclusions reached in referenced articles).

a. Grassi, *Inferior Vena Caval Filters: Analysis of Five Currently Available Devices*. 1990.
    i. "Further clinical trials of these devices with randomized prospective study are necessary, in order to further refine the existing filters and to assist in the development of a filter that will be superior for the prevention of PE. Until that time, the choice of an IVC filter from

those available should be based not only on the IR's preference, but also on the specific clinical situation and the filter's performance."

b. Becker, *Inferior vena cava filters: indication, safety, effectiveness.* 1992.
   i. Variable filter safety and effectiveness requires matching the best filter to a particular situation, a decision process that should involve the physician taking care of the patient and the physicians who insert the device."

c. Dorfman, *Percutaneous inferior vena caval filters*. 1990.
   i. Until a multicenter, randomized, prospective trial is initiated, there should be a mandatory registry of all patients who filters are placed. This could be supported by the manufacturers and supplies of the devices and be maintained by an independent scientific body.

d. Magnant, *Current Use of Inferior Vena Cava Filters*, 1992.
   i. "Ongoing clinical studies of large patient populations will be useful in determining specifically which patient subgroups are most likely to benefit from filter placement."

e. Greenfield, *Results of long-term venacavography study after placement of a Greenfield vena caval filter,* 1992.
   i. "What should the hypothetical physician do?... Explain that available information is incomplete.
   ii.

219. Table 2 does not contain any thresholds, and reported incidences are defined as "other trackable events". A review of the sources of those reported failures demonstrates the limitations of a meta-analysis medical literature study. For example, the fracture failure rate is based upon two studies by a team of University of Arkansas doctors, (Complications of the Nitinol Vena Caval Filter, JVIR 1992; 3:401-408), in 1992 and 1993. The 1992 paper studied twenty (20) patients and found two (2) fractures, providing a 10% failure rate reported in the article. The same team expanded the study to three hundred and twenty (320) patients for the 1993 article and found a 2% fracture rate, providing the 2% failure rate contained in Table 2. The two studies were limited to one hospital that used **older permanent filters** from between 1985-1992.

220. **No medical literature review of retrievable filters until 2017:** The data evaluated in the medical literature for the 2003 and 2011 articles involved past studies, none of which involved retrievable filters. None of the updates to the SIR paper has reviewed or added any new medical literature to the fracture rates reported in Table 2 – until 2017 (see ACR-SIR-SPR Practice Parameter referenced, below). None of the studies reported on retrievable filters, nor to design changes on older devices, or the elimination of certain devices no longer being marketed and used between 1992 and 2003. Nor the emergence of newer designed devices.

221. The 2017 revision of the SIR article, (ACR–SIR–SPR Practice Parameter for the Performance of Inferior Vena Cava (IVC) Filter Placement For The Prevention Of Pulmonary Embolism (Revised 2016 (Resolution 18), available at https://www.acr.org/~/media/a569be8f18ae4cfaa2868b6e0984dbd8.pdf, last visited 1/27/17), indicates that the reported rate for penetration is 0-100%, for migration, 0-25%, and for fracture, 0-50%. The broad ranges in the table characteristically indicate that this data is a qualitative review of the available medical literature and there should be no consideration that this represents a SIR supported industry standard. The most persuasive evidence of SIR's intent has been added to the comment below Table 2: "The data in the table represents reported outcomes from various publications and not the SIR standard for complications." SIR confirms that Table 2 does not represent industry standards for failure rates. It certainly goes without saying that physicians are more likely going to choose the devices where these trackable events are at or closest to the 0% of these reported ranges

222. **SIR disclaimer states "these guidelines are voluntary and are not rules"**: In 2003 and 2011 SIR articles, the Standard Committee added a disclaimer as a further illustration of the intention of the authors: "The clinical practice guidelines of the Society of Interventional

Radiology attempt to define practice principles that generally should assist in producing high quality medical care. These guidelines are voluntary and are not rules."

223. **No medical organization establishes "acceptable thresholds" for complication rates:** SIR, ACR or any other medical organization have made no representations that it supports acceptable thresholds as related to and associated with IVC filters design, track record of complication rates, or malfunction or related injuries to patients. The SIR Standards Committee articulated this position in the 2011 article, "[t]he Committee is unable to reach consensus on the following: Indication, efficacy, or complication *threshold*." It is clear; the SIR articles do not purport to establish thresholds for failures rates, specifically for fracture, migration, and perforation.

B. The Purpose of the Society of Interventional Radiology *Quality Improvement Guidelines*

224. The Society of Interventional Radiology, through member participants of the Standards of Practice Committee, including Anne Roberts, MD a contributing author to this report, published article in the Journal of Vascular Interventional Radiology titled Quality Improvement Guidelines for Percutaneous Permanent Inferior Vena Cava Filter Placement for the Prevention of Pulmonary Embolism in 2001 (and republished 2003). The underlying data used to perform the meta-analysis studied only older model permanent IVC filters as retrievable filters were not available until 2003. The first author named in of this article is Clement Grassi, M.D., and, as such, this quality improvement article is often referred to as the "Grassi Article".

225. With advances in technology and design, manufacturers began developing "retrievable" or "option" filters. In 2011, Dr. Kalva, along with fellow Standards of Practice Committee member, updated the guidelines, Quality Improvement Guidelines for Percutaneous

Permanent Inferior Vena Cava Filter Placement for the Prevention of Pulmonary Embolism, in collaboration with the American College of Radiology (ACR) to include additional instruction and education related to permanent filters with options for retrieval. This update was effectuated to provide practitioners with instructional guidance related to retrievable filters and, for some sections of the article, it did not involve review of additional or current medical literature relating to the "other trackable events" section of the article.

226. These articles are instructional in nature, providing technical requirements for examination equipment and facilities, placement techniques, pre- and post procedure care, physiologic monitoring and resuscitation equipment, patient selection, monitoring the patient and threshold complication rates; specifically, to illustrate the intent of the article: "[t]hese guidelines are written to be used in quality improvement programs to access percutaneous interruption of the IVC to prevent."

227. The Society of Interventional Radiologist regularly publishes guidelines for establishing quality improvement programs in interventional radiology and further illustrates the educational context of the guidelines related to IVC filters. SIR describes their intent in the introduction of *Quality improvement programs in interventional radiology*. J Vasc Interv Radiol 2010; 21:617– 625.

> a. Quality is not a static goal but a progressively improving state, and interventional radiology is a rapidly moving, technology-driven subspecialty in which high-quality patient care should be the norm. The health care we deliver next year must be better than the health care we deliver today. In order to attain such essential goals, interventional radiology must initiate specialty wide continuous quality improvement (CQI) programs. Ensuring high-quality patient care in interventional radiology is a primary goal and responsibility of the Society of Interventional Radiology (SIR).

228. As such, the "Quality Improvement" article related to IVC filters was not published as guideline statement for acceptable threshold and complication rates of IVC filters.

Establishing acceptable thresholds for safety for IVC filter manufacturers was not the intent of the authors or SIR. As stated in the article "indicator thresholds may be used to access the efficacy of ongoing quality improvement programs." The article was not intended to be used by IVC filter manufacturing companies but, instead, was intended to be used by hospitals and physicians in their "quality assurance" programs and does not purport to provide an acceptable range of complication rates for manufacturers.

229. Dr. Clement Grassi, the first named author of the 2001 SIR article (republished in 2003) and retained expert witness for Bard, testified that the article should not be used and was not intended to be used to indicate safety thresholds (Grassi Depo., Aug 22 2013, 59:2-19). As stated in the article, the data presented should only have been used to identify several types of complications associated with IVC filters that should be tracked ("Other Trackable Events"). The calculations referenced in the article were not intended as thresholds for safety but rather as indicators for when quality assurance mechanisms should be initiated at hospitals. It is our opinion, the SIR "Quality Improvement" article is not to be used as design parameters, acceptability of statistically significantly higher reporting rates among filters, justification for keeping an admittedly design-flawed device on the market while being redesigned to deal with those flaws and unexpected, unintended and inordinately higher complications of an existing device, or to avoid all reasonable steps expected of an IVC Filter manufacturer to test, design and ensure they are putting the safest and most effective device on the market, such as Bard did with its IVC filters, but rather for individual practitioner evaluation.

230. The intent of these guidelines is illustrated by the following statement: "These guidelines are written to be used in quality improvement programs to assess percutaneous interruption of the IVC to prevent pulmonary embolism. The most important processes of care

are (a) patient selection, (b) performing the procedure, and (c) patient monitoring. The outcome measures or indicators for these processes are indications, success rates, and complication rates. Outcome measures are assigned threshold levels." The article continues with: "For simplicity, these guidelines will not suggest threshold (complication) rates for each individual filter; rather, filtration devices will be considered as a group (Table 1)."

Table 1 "Complications" 2003):

Table 1
Complications

Complications	Reported Rates (%)	Threshold (%)
Death (7)	0.12	<1
Recurrent PE (17–22)	0.5–6	5
IVC Occlusion (11,17,19,20,23–27)	2–30	10
Filter Embolization (17,24,28–37)	2–5	2
Access Site Thrombosis—Major (see Appendix 1) (38,39)	0–6*	1

* Includes reported rates of both major and minor complications.

Quality Improvement Guideline for the Performance of Inferior Vena Cava Filter Placement for Prevention of Pulmonary Embolism, J Vasc Interv Radiol 2003; 14:S271 –S275.

Table 1 "Reported Rats and Thresholds for Complications" (2011):

Table 1. Reported Rates and Thresholds for Complications (7,24,37–54)

Complication	Reported Rate (%)	Threshold (%)
Death (7)	0.12	<1
Filter embolization (24,37–49)	0.1	1
Deployment outside target area (50–52)	1–9	0
Access site thrombosis/ occlusion (53,54)	3–10	3

Quality Improvement Guideline for the Performance of Inferior Vena Cava Filter Placement for Prevention of Pulmonary Embolism, J Vasc Interv Radiol 2011; 22:1499-1506.

231. Dr. Grassi recognized that “published rates for individual types of complications are highly dependent on patient selection and are, in some cases, based on series comprising several hundred patients, which is a volume larger than most individual practitioners are likely to treat. It is also recognized that a single complication can cause a rate to exceed a complication-specific threshold when the complication occurs in a small volume of patients, for example, early in a quality improvement program.” *Quality Improvement Guideline for the Performance of Inferior Vena Cava Filter Placement for Prevention of Pulmonary Embolism*, J Vasc Interv Radiol 2011; 22:1499-1506.

232. “Because an IVC filter is a permanent implantable device and because this device is sometimes placed in relatively young patients, several other trackable parameters when observed are appropriate to record in a quality improvement program. The events listed in **Table 2** may or may not be clinically significant in a particular patient. For this reason, thresholds for these events are not included in this document**.”** “*Quality Improvement Guideline for the Performance of Inferior Vena Cava Filter Placement for Prevention of Pulmonary Embolism*,” J Vasc Interv Radiol 2011; 22:1499-1506.

Table 2. "Other Trackable Events" (2003)

Table 2
Other Trackable Events

Other Trackable Events	Reported Rates (%)
IVC Penetration (7,17,19,23,27,40,52)*	0–41
Migration (7,9,10,17,19–21,26,41,42)*	0–18
Filter Fracture (17,24)	2–10
Access Site Thrombus	
All types (7,38,43,44)	0–25
Occlusive (38,45)	3–10
Insertion Problems (7,17,19–22,24,26,41,43,46,47)	5–50
Other complications (48,49)	1–15

Note.—The rate of clinically significant penetration is undefined in the literature (39,50,52).
* Clinically significant penetration and migration are believed to be rare.

Table 2. "Trackable Adverse Events" (2011)

Table 2. Reported Incidences of Trackable Adverse Events (2,7,10,12,13,24,43,53,55–72)

Event	Reported Rate (%)
IVC penetration*(7,24,55–59)	0–41
Filter movement*(7,10,12,24,56,60–63)	0–18
Filter fracture (24,43)	2–10
Recurrent PE (24,56,61,53–65)	0.5–6
Access site thrombus, all types (7,53,64,65)	0–25
IVC occlusion (13,24,42,55,56,59,62,63,68)	2–30
Insertion problems (7,24,43,56,51–63,65,67,69,70)	5–23
Other complications (2,71,72)	1–15

Note.—The rate of clinically significant penetration is undefined in the literature (39,50,52).* Clinically significant penetration and migration are believed to be rare.

233. Dr. Grassi, in his deposition, states that these are not to be used as design parameters such as Bard did in their analysis but rather for individual practitioner evaluation.

> a. "And certainly I can say that in the quality improvement guidelines for IVC filter placement through SIR for which I was the first author, we did not imply that rates in that range are fine or acceptable or okay. We simply said that those were trackable events and that responsible individuals should look at any adverse event, trigger a review, and do a quality assurance monitoring to make sure that they understand some root causes behind such a serious problem."
>
> (Deposition of Dr. Clement Grassi, August 27, 2014, 525-526:14-1)

234. Dr. Grassi also testified that for an investigation of adverse events for Bard's IVC filters: "He would want to know the summary of an investigation….Well, what I can say in the general sense is that personally and many of my colleagues would logically seek the device with the greater benefit and the fewer risks or complications. (Deposition transcript of Dr. Clement Grassi, August 27, 2014 534-535:16-21).

235. Similarly, performance standards have evolved from the Society of Interventional Radiology (SIR), American College of Radiology (ACR) and SPR (Society of Pediatric Radiology). The latest standard was just updated in 2016. In the preamble to this document it is stated: This document is an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. Practice Parameters and Technical Standards are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the American College of Radiology and our collaborating medical specialty societies caution against the use of these documents in litigation in which the clinical decisions of a practitioner are called into question. It is recognized that- Although retrievable filters are often placed as permanent devices, the long-term safety and efficacy of these devices as a class have not been established. However,

all retrievable convertible filters are cleared for permanent placement. It is stated-These practice parameters are intended to be used in quality improvement programs to assess percutaneous interruption of the IVC to prevent PE. The most important aspects of care are 1) patient selection, 2) performing the procedure, and 3) monitoring the patient. The outcome measures or indicators for these processes are indications, success rates, and complication rates. Outcome measures are assigned threshold levels. Few comparative studies have been completed evaluating all filters in one project, and those that have done so have been retrospective analyses. Complication rates are highly variable depending on the filter being studied. For simplicity, these practice parameters do not suggest threshold rates for each individual filter; rather, filtration devices are considered as a group.

TABLE 1

Complications	Reported Rates (%)	Threshold (%)
Death [52]	0.12	< 1
Filter embolization [9,32,45,46,53-65]	0.1	1
Deployment outside target area [34,66,67]	1-9	<1%
Access site thrombosis occlusive [68,69]	3-10	3

Published rates for individual types of complications are highly dependent on patient selection and are in some cases based on series comprising several hundred patients, which is a volume larger than most individual practitioners are likely to treat. It is also recognized that a single complication can cause a rate to cross above a complication-specific threshold when the complication occurs within a small patient volume (eg, early in a quality improvement program).

TABLE II: Other Trackable Events

TABLE II

Other Trackable Events	Reported Rates (%)
IVC penetration* [7,10,12,13,15,16,21,32-39,42,51,52,58,59,61,63,65,67-76]	0-100
Migration of filter/filter components* [10,11,13,16,18,19,21,24,31,32,34,36,40-43,45,52,55,56,63,65,67,70-85]	0-25
Filter fracture [9-17,21,32,34,37,39,51,53,54,58,60-62,66,71-74,76,78,80,81,83-86]	0-50
Recurrent PE [32,71,72,78,82]	0.5-6
Access site thrombus – all types [52,68,83,84,86]	0-25
IVC occlusion [12,14,15,20,26,27,30,32,34,36,41,43-46,51,56-58,61,69-77,79,82,85,87,88]	2-65
Insertion problems [32,52,61,71,72,78,79,82,84,87,88]	5-23
Other complications [2,75]	1-15

The data in the table represents reported outcomes from various publications and not the SIR standard for complications.

* The rate of clinically significant penetration is not precisely known [85].

See ACR-SIR, *SPR Practice Parameter for the Performance of Inferior Vena Cava (IVC) Filter Placement for the Prevention of Pulmonary Embolism*, 2016 (rev. 2017).

236. Therefore, these documents are for practicing physicians to monitor their own programs of quality improvement and assurance and not to be used for design parameters for medical devices or for clearance of such devices by Federal Bodies (FDA). In our opinion, most physicians would like to see devices have no complications but this is not always possible. However, striving for the lowest possible complications and achieving the desired goals are expected. It is hoped that continued progress in evolution of devices will result in ever decreasing instances of complications.

X. BARD'S IMPROPER USE OF THE SIR QUALITY IMPROVEMENT GUIDELINES

237. Due to the methodological limitations addressed, it is inappropriate for Bard to use the cited Tables for comparisons between their devices and other marketed devices. The SIR

"Quality Improvement" article was repeatedly taken out of context by Bard in its QA documents, communications with FDA, and with its own sales force. As such, Bard's use of the article for comparison "thresholds," or to advance a corporate-cleared message that their devices have acceptable failures, complications, malfunctions, adverse events (serious injuries and death) is misleading for both clinicians and their sales force to rely upon.

238. Bard's comparison of their own adverse event reports to complication rates in the SIR article rates was inappropriate, confusing, and grossly misrepresented the rate of complication rates that were expected and acceptable for Bard's filters.

239. By example, in the review article Thomas Kinney wrote in 2003, only permanent IVC filters were commercially available in the U.S. The permanent filters had accumulated a relatively long- series of performance data mostly via case series. In that article, a table was included which listed the attributes of an ideal IVC filter:

Table 1
Desirable Attributes of an "Ideal" Filter (Ref. 21 - Grassi CJ. *Inferior vena caval filters: analysis of five currently available devices*. AJR Am J Roentgenol 1984; 151:525-6)

- Nonthrombogenic, biocompatible, infinite implant lifetime performance
- High filtering efficiency (large and small emboli) with no impedance of flow
- Secure fixation within the IVC Ease of percutaneous insertion
- Small caliber delivery system
- Release mechanism simple and controlled
- Amenable to repositioning
- MR imaging compatibility
- Low cost
- Low access site thrombosis
- Retrievability

240. At that time, physicians were seeking filters that could be removed when a patient was no longer at risk for DVT/PE. However, secure fixation was recognized as being an important criterion. As an example of complications reported for permanent filters is illustrated by the following table from the Article (J Vasc Interv Radiol 2003: 14:425-40).

Table 4
Complications Reported with Use of IVC Filters (Ref. 57- Ray CE, Kaufman JA. *Complications of inferior vena cava filters.* Abdom Imaging 1996; 21:368-74;58- Ballew KA, Philbrick JT, Becker DM. Vena Cava filter devices. Clin Chest Med 1995; 16:295-305)

Complication	**Rate (%)**
Pulmonary embolism	2–5
Fatal pulmonary embolism	0.7
Death linked to insertion of an IVC filter	0.12
Complications from insertion*	4–11
Venous access site thrombosis	2–28
Migration of the filter	3–69
Penetration of the IVC†	9–24
Obstruction of the IVC	6–30
Venous insufficiency‡	5–59
Filter fracture	1
Guide wire entrapment	<1

* Complications from insertion include puncture site complications such as bleeding, infection, pneumothorax, vocal cord paralysis, stroke, delivery system complications; air embolism; and filter malposition, tilting, or incomplete opening.

† Penetration of the IVC, which can occur immediately, but is more commonly seen as a delayed sequela. Most often, patients are asymptomatic from such IVC penetrations; however, untoward events have been described by penetration of filter struts into small bowel, aorta, and sympathetic ganglia.

‡ Most reports of IVC filters usually report venous insufficiency rates as less than 10%. When studies are conducted for longer periods of follow-up (as long as 6 years), more than 58.8% of patients may have clinical signs of venous insufficiency. The data are somewhat controversial because as many as 30%– 45% of patients treated with anticoagulation therapy may experience venous insufficiency after follow-up of 6 years.

241. Figures such as these are collected from case series and include all types of filters including devices which are no longer used and encompasses a wide time-frame of study. The upper numbers do not reflect desirable performance characteristics as ideally the rates should be as low as feasibly possible. These are not construed to represent design constraints for manufacturers of devices but for physician information about performance characteristics that have been reported with current and previously available devices.

242. [redacted]

243. [redacted]

244. It is misleading for Bard to use the SIR article complication rates to interpret their high rates of adverse events associated with the Recovery and G2 filters as being acceptable. It is misleading and erroneous for Bard to suggest to doctors or the public that the SIR article's upper limit of 10% for fracture complication rates represents a reasoned consensus among interventional radiologists for fracture rates, or that it this rate has any application to acceptable failure rates for retrievable filters; Bard knows this rate is based on a single study of twenty (20) patients using permanent filters that ended in 1992.

245. One example, an FDA Contact Report dated January 21, 2005 written by Shari Allen, VP of Regulatory at Bard, recorded a conversation she had with FDA's Lisa Kennell. Allen indicated that she told Kennell, that Bard's proposed IFU changes in the previous

communication to FDA had been implemented and the customer communication letter was distributed. She reportedly told Ms. Kennell that:

> **a.** …***all adverse event reporting rates (e.g. migration, fracture, etc.) had remained the same or below the rates identified in October 2004, "Event Comparison Chart" and that there were well below the rated described in the Society of Interventional Radiology (SIR) Quality Improvement Guideline.***

246. This is an inaccurate representation to FDA and Ms. Kennell since SIR Quality Improvement Guideline has "no deaths reported for an embolized IVC filter," the only reported IVC filter deaths were embolization of thromboembolism at the time of the implant procedure.

247. Allen continued to use the SIR "Quality Improvement" article along with Bard's use of the FDA's MAUDE database to support that it was the 'bariatric surgery patients' that appeared to be skewing the risk of migration (embolization) deaths for the Recovery Filter, and without those 'bariatric patients' the Recovery filter was just as safe as competitor filters.

248. Ms. Allen did not indicate to Ms. Kennell, which would have been relevant to a reviewer in ODE that the Recovery Filter was not performing as safely and effectively as purported in its cleared 510(k) and was not SE to Bard's SNF. Also, Bard would have been aware that it Recovery Filter was not performing as safely and effectively as any of the five cleared permanent filters discussed in Streiff (2000).

249. Instead, Ms. Allen wrote that she told Ms. Kennell, that improper physician use, the subject of the 2004 IFU change and Dear Doctor letter, of Recovery Filters in bariatric patients was the etiology of all the problems with the Recovery device. Other than improper physician use, the Recovery Filter performed just like all other cleared IVC filters.

250. [redacted]

[redacted]

251. [redacted]

252. As practicing physicians with patients who are candidates for IVC filter, or have them implanted, we would expect Bard to redesign their filters upon review of this comparison which demonstrates a high complication rates associated with both the Recovery and the G2 filters. Specifically, rates of death, PE, and fracture were statistically significantly, higher than the next ranked filter, including the predicate, SNF.

253. Bard was using "threshold" and "trackable events" levels in the SIR article for comparison with the event rates that were being observed with the Recovery and G2 filters. It is our opinion that in no way do these rates reflect a consensus of opinion among interventional radiologists as to what should be expected or accepted.

XI. DR. KALVA'S EXPERIENCE AT MASSACHUSETTS GENERAL HOSPITAL EXPERIENCE, HIS INTERACTIONS WITH BARD AND THE FAILURE OF BARD TO DISCLOSE HIGHLY RELEVANT AND IMPORTANT INFORMATION

A. Experience with the Recovery Filter

254. My initial experience with Bard's first generation Recovery inferior vena cava filter occurred when I was a member of the Department of Radiology at Massachusetts General Hospital; a Harvard affiliated hospital, in Boston. This was the first removable filter that was available for use in the United States. At that time, Bard aggressively marketed its Recovery filter as both safe and effective for permanent and temporary implantation. For example:

a. Recovery Brochure

b. Bard's brochure for the Recovery Vena Cava Filter touts its filter safety and effectiveness in a variety of important ways stating that: the filter has a "Timeless Performance;" that it is "Designed To Be The Only Filter You Will Ever Need;" that Bard has "Leveraged" its "Decade-Long Experience To Bring You The Next Generation In Filter Performance;" that Recovery's "Self-Centering Design, Proven Conical Shape And Bi-Level Filtering System Create The Ideal Balance Between Clot Trapping Efficiency And Caval Patency;" that Recovery's "Advanced Design And Accurate Placement Coupled With Lasting Performance Making Recovery The Permanent Solution To Caval Interruption;" there is "Secure Fixation" of the filter to the inferior vena cava; and, that the Recovery filter is a "Marked Improvement Over Currently Available Devices" (which would include Bard's own Simon Nitinol Filter). (BPV-17-01-00007760 – 7763).

255. The above representations made by Bard to me and to the public/medical community, never changed while the Recovery filter was available for use in the United States. These safety features were very important and desirable to me in deciding to use this filter and implant it in my patients.

256. While at Massachusetts General Hospital, my colleagues and I, to include Stephan Wicky, M.D., began to observe safety issues related to the Recovery filter. I was particularly concerned about penetrations of the legs of the filter through the vena cava. This raised safety concerns because these leg penetrations were in close proximity to the aorta and other vital organs.

257. These failures of the Recovery filter raised serious concerns about the safety of this filter. This alarming revelation and my concerns were reported to Bard (Robert Carr, Janet Hudnall and Bob Scherer) in June – July of 2005. I, along with Dr. Wickey, requested that Bard, with the assistance of me and my colleagues, perform a study to assess the safety of the Recovery filter for the health and well-being of patients already implanted with the Recovery filter, for those yet to be implanted with this filter, and to determine whether this filter model posed an unacceptable risk to patients who were in need of an inferior cava filter. This study was particularly important for those patients already implanted with the Recovery filter so that follow-up and appropriate treatment decisions could be made once a study to assess the safety profile of the filter was completed. This safety study could not be performed without the assistance of and funding from Bard.

B. <u>Discussions with Bard Representatives and Internal Emails To Derail Efforts to Conduct a Safety Study of the Recovery Filter</u>

258. Despite our concerns, Bard was not willing to provide assistance or funding for the safety study referred to above. I recently had an opportunity to see some of Bard's internal emails and learned for the first time that Bard had intentionally developed a plan to derail our desire to perform a safety study of the Recovery filter as it was a lose/lose proposition for Bard.

This decision by Bard was without regard for the safety and well-being of the many patients implanted with the Recovery filter.

C. Massachusetts General Hospital Study

259. Our studied examined 40 of 96 patients who were implanted with the Recovery filter. The patients studied (40) had all undergone contrast enhanced CT imaging of the abdomen. We found an unacceptably high failure rate in these patients following a relatively short period of time after implantation of the Recovery filter. This finding was contrary to the statements made in the Recovery filter brochure and representatives of Bard. CT imaging demonstrated tilt (asymmetrically deployed legs or clumping of the filter legs) of the filter in 30% of the patients (12 of 40 patients); penetration/perforation of the inferior vena cava by the filter arms was seen in 27.5% of the patients (11 of the 40 patients) and in 5 of those 11 patients, the arms of the filter were penetrating into adjacent vital organs, in 2 of those 11 patients, the filter arms were dangerously close to the aorta, and in 3 of those 11 patients, pieces of the filter had fractured with one of the fractured pieces migrating to the pancreas. Each of these failure modes pose a risk of immediate or delayed injury and/or death to those patients implanted with a Recovery filter.

D. Bard's Was In Possession of Substantial Information Of Unacceptable Safety Problems With The Recovery Prior To My Experience At Massachusetts General Hospital And Bard's Failure To Disclose This Unacceptable Safety Profile

[redacted]

[redacted]

261. [redacted]

262. [redacted]

263. [redacted]

264. [redacted]

[redacted]

265. [redacted]

266. [redacted]

267. [redacted]

[redacted]

[redacted]

268. [redacted]

[redacted]

[redacted]

[redacted]

269. [redacted]

270. [redacted]

[redacted]

271. I, along with those physicians who order the implantation of filters and those who implant filters, would expect a device manufacturer to convey to the medical community this crucial information for the health, well-being and safety of patients that need a filter. In addition, I would have expected Bard to have conveyed this information to me after I reported to Rob Carr

and others high and unacceptable rate of failures my colleagues and I experienced with the Recovery filter while at Massachusetts General Hospital.

272. Recovery reporting rates for all adverse events, filter fracture, filter migration and filter migration deaths were found to be statistically significantly higher than those for other removable filters.

273. It is evident that while Bard knew a filter could be designed to lessen these occurrences, as is shown by the lower reporting rates all other filters, including removable filters, Bard chose to continue selling and profiting from the current design at the risk of the health, safety and wellbeing of patients in need of a filter.

274. [redacted]

[redacted]

275. This critical inquiry should sound off alarms, as the "user" may treat for a differential diagnosis, allowing further damage by the filter to the "user." This information that is not otherwise known to the user should have been conveyed in order for the physician and

his/her patient to perform an informed risk/benefit analysis to determine whether a filter should be implanted and, if so, which brand filter should be selected for implantation.

[redacted]

276. [redacted]

277. [redacted]

[redacted]

278. [redacted]

279. An a final example, CardioVascular and Interventional Radiology, March 24, 2006, "*Recovery" Vena Cava Filters: Experience in 96 Patients*, Sanjeeva P. Kalva, Christos A. Athanasoulis, Chieh-Min Fan,, Marcio Curvelo, Stuart C. Geller, Alan J. Greenfield, Arthur C. Waltman,, Stephen Wicky.

a. An unacceptable adverse event rate at Mass General.

b. This was information known to Bard long before Dr. Kalva's experience at Mass General; this failure rate is unacceptable - exposes patients to an unacceptable risk without informed consent.

c. Informed consent is a two-step process – the doctor has to be adequately advised of the device before they use the device, and that information has to be imparted ultimately to the patient so they can make an informed decision.

d. When companies like Bard withhold that crucial information, the doctors and patients are uninformed about the utility and risks of the device, and therefore, there is no informed consent.

XII. CONCLUSION

280. This expert report was a collaborative effort among the authors, similar to the methodology employed had we been contributing to a medical article, professional society guidance or practice parameters document, or presentation to the medical community, or to professional societies and organizations, like the Society of Interventional Radiologists and the American College of Radiology.

281. Our expert opinions are to a reasonable degree of medical probability and based on standard of care principles and practices, as those relate to the expectations of what a reasonable physician, reasonable members of our professional societies, and reasonable consultants to medical device companies would want, need and expect from data and information possessed by medical device companies like Bard, and especially in the context of IVC filters, both prior to and after their products are released into the open market.

282. Our expert opinions are to a reasonable degree of medical probability and grounded on standard of care principles that would permit proper, complete and fact-based informed consent obligations to patients who are deemed to be candidates for IVC filtration, and obligations to physicians involved in these decisions to be sufficiently and continually informed by manufacturers and sellers IVCF devices of the data and information they possess that are important to physicians in making appropriate therapeutic decisions on behalf of their patients where an IVC filter may be indicated or considered as a therapeutic option.

XIII. SIGNATURES

Thomas Kinney, M.D., M.S.M.E.

Signed this 6th day of March, 2017

Thomas Kinney, M.D., M.S.M.E.

Anne Roberts M.D.

this 6th day Signed of March, 2017

Anne Roberts M.D.

Sanjeeva Kalva M.D.

Signed this 6th day of March, 2017

See attached signature

Sanjeeva Kalva M.D.

Anne Roberts M.D.

Signed this 6th day of March, 2017

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Anne Roberts M.D.

Sanjeeva Kalva M.D.

Signed this 6th day of March, 2017

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Sanjeeva Kalva M.D.